```
=> d his

     (FILE 'HOME' ENTERED AT 10:40:20 ON 06 JAN 2005)

     FILE 'REGISTRY' ENTERED AT 10:40:28 ON 06 JAN 2005
               E "DNASE"/CN 25
L1           10 S E3 OR E25 OR E31 OR E34 OR E43 OR E51 OR E52 OR E55 OR E56 OR

     INDEX '1MOBILITY, 2MOBILITY, ABI-INFORM, ADISCTI, AEROSPACE, AGRICOLA,
     ALUMINIUM, ANABSTR, ANTE, APOLLIT, AQUALINE, AQUASCI, AQUIRE, BABS,
     BIBLIODATA, BIOBUSINESS, BIOCOMMERCE, BIOENG, BIOSIS, BIOTECHABS,
     BIOTECHDS, BIOTECHNO, BLLDB, CABA, CANCERLIT, ...' ENTERED AT 10:47:05 ON
     06 JAN 2005
               SEA DNASE OR EXONUCLEASE OR (CASPASE (W) ACTIVATED (W) (DEOXYRI
              ---------
              36   FILE ABI-INFORM
              82   FILE ADISCTI
              23   FILE AEROSPACE
            3412   FILE AGRICOLA
               1   FILE ALUMINIUM
             132   FILE ANABSTR
              10   FILE ANTE
              17   FILE APOLLIT
              25   FILE AQUALINE
             880   FILE AQUASCI
             513   FILE BABS
              37   FILE BIBLIODATA
             788   FILE BIOBUSINESS
             311   FILE BIOCOMMERCE
            2337   FILE BIOENG
           43137   FILE BIOSIS
            6953   FILE BIOTECHABS
            6953   FILE BIOTECHDS
           23129   FILE BIOTECHNO
            6799   FILE CABA
           10395   FILE CANCERLIT
              28   FILE CAOLD
           53112   FILE CAPLUS
             102   FILE CASREACT
             170   FILE CBNB
             669   FILE CEABA-VTB
              24   FILE CEN
               5   FILE CHEMINFORMRX
              98   FILE CIN
               6   FILE CIVILENG
             651   FILE COMPENDEX
              17   FILE COMPUAB
              12   FILE COMPUSCIENCE
             664   FILE CONFSCI
               4   FILE CROPB
              84   FILE CROPU
               4   FILE CSNB
             130   FILE DDFB
             688   FILE DDFU
           31785   FILE DGENE
            3171   FILE DISSABS
             388   FILE DPCI
             130   FILE DRUGB
            1281   FILE DRUGU
               2   FILE ELCOM
               1   FILE EMA
             183   FILE EMBAL
           30398   FILE EMBASE
            1839   FILE ENERGY
```

```
         9   FILE ENTEC
         9   FILE ENVIROENG
     11560   FILE ESBIOBASE
        25   FILE FRANCEPAT
       610   FILE FRFULL
       167   FILE FROSTI
       712   FILE FSTA
    107118   FILE GENBANK
         1   FILE GEOREF
        49   FILE HEALSAFE
      3746   FILE IFIPAT
        41   FILE IMSDRUGNEWS
      1024   FILE INIS
      1793   FILE INPADOC
       257   FILE INSPEC
        33   FILE INSPHYS
       564   FILE INVESTEXT
        76   FILE IPA
       252   FILE JAPIO
      3877   FILE JICST-EPLUS
        35   FILE KOREAPAT
        27   FILE KOSMET
     21206   FILE LIFESCI
         1   FILE MATBUS
         9   FILE MATH
         6   FILE MATHDI
         2   FILE MECHENG
     39564   FILE MEDLINE
         1   FILE METADEX
        22   FILE NAPRALERT
       148   FILE NIOSHTIC
       557   FILE NLDB
       313   FILE NTIS
       199   FILE OCEAN
        24   FILE PAPERCHEM2
     13491   FILE PASCAL
         6   FILE PATDD
        97   FILE PATDPA
      1852   FILE PATDPAFULL
     26560   FILE PCTFULL
        33   FILE PHARMAML
       106   FILE PHIN
         1   FILE PIRA
        44   FILE POLLUAB
       655   FILE PROMT
         9   FILE RAPRA
     28079   FILE SCISEARCH
        39   FILE TEMA
         6   FILE TEXTILETECH
     18348   FILE TOXCENTER
         2   FILE TULSA
         3   FILE UFORDAT
        21   FILE ULIDAT
     41134   FILE USPATFULL
      2145   FILE USPAT2
         1   FILE VETB
       117   FILE VETU
        45   FILE WATER
      3071   FILE WPIDS
        15   FILE WPIFV
      3071   FILE WPINDEX
         5   FILE WTEXTILES
L2           QUE DNASE OR EXONUCLEASE OR (CASPASE (W) ACTIVATED (W) (DEOXYRI
             ---------
```

SEA DNAASE OR DORNASE OR DORNAVA OR DORNAVAC OR ENDONUCLEASE

11	FILE ABI-INFORM
91	FILE ADISCTI
17	FILE AEROSPACE
2742	FILE AGRICOLA
58	FILE ANABSTR
6	FILE ANTE
9	FILE APOLLIT
13	FILE AQUALINE
646	FILE AQUASCI
267	FILE BABS
8	FILE BIBLIODATA
517	FILE BIOBUSINESS
144	FILE BIOCOMMERCE
1697	FILE BIOENG
25106	FILE BIOSIS
5814	FILE BIOTECHABS
5814	FILE BIOTECHDS
16016	FILE BIOTECHNO
5202	FILE CABA
5545	FILE CANCERLIT
12	FILE CAOLD
30616	FILE CAPLUS
35	FILE CASREACT
49	FILE CBNB
476	FILE CEABA-VTB
11	FILE CEN
2	FILE CHEMINFORMRX
46	FILE CIN
2	FILE CIVILENG
331	FILE COMPENDEX
17	FILE COMPUAB
1	FILE COMPUSCIENCE
450	FILE CONFSCI
4	FILE CROPB
75	FILE CROPU
3	FILE CSNB
111	FILE DDFB
462	FILE DDFU
24812	FILE DGENE
1753	FILE DISSABS
294	FILE DPCI
111	FILE DRUGB
767	FILE DRUGU
1	FILE ELCOM
101	FILE EMBAL
20527	FILE EMBASE
1417	FILE ENERGY
5	FILE ENTEC
5	FILE ENVIROENG
6309	FILE ESBIOBASE
17	FILE FRANCEPAT
387	FILE FRFULL
130	FILE FROSTI
626	FILE FSTA
54466	FILE GENBANK
43	FILE HEALSAFE
2589	FILE IFIPAT
34	FILE IMSDRUGNEWS
786	FILE INIS
1137	FILE INPADOC
174	FILE INSPEC
19	FILE INSPHYS

```
   125   FILE INVESTEXT
    85   FILE IPA
   160   FILE JAPIO
  2311   FILE JICST-EPLUS
    21   FILE KOREAPAT
    26   FILE KOSMET
 14210   FILE LIFESCI
     5   FILE MATH
     1   FILE MECHENG
 22312   FILE MEDLINE
    10   FILE NAPRALERT
    96   FILE NIOSHTIC
   390   FILE NLDB
   228   FILE NTIS
   162   FILE OCEAN
    18   FILE PAPERCHEM2
  9748   FILE PASCAL
     4   FILE PATDD
    34   FILE PATDPA
   601   FILE PATDPAFULL
 20303   FILE PCTFULL
    80   FILE PHARMAML
   141   FILE PHIN
    34   FILE POLLUAB
   409   FILE PROMT
     1   FILE RAPRA
 18200   FILE SCISEARCH
    15   FILE TEMA
     4   FILE TEXTILETECH
 10614   FILE TOXCENTER
     2   FILE TULSA
     1   FILE UFORDAT
    10   FILE ULIDAT
 32655   FILE USPATFULL
  1620   FILE USPAT2
     1   FILE VETB
   109   FILE VETU
    23   FILE WATER
  2134   FILE WPIDS
    11   FILE WPIFV
  2134   FILE WPINDEX
     3   FILE WTEXTILES
L3       QUE DNAASE OR DORNASE OR DORNAVA OR DORNAVAC OR ENDONUCLEASE
         ---------
         SEA (L2 OR L3) (30A) HUMAN
         ---------
     3   FILE ABI-INFORM
    27   FILE ADISCTI
     2   FILE AEROSPACE
    53   FILE AGRICOLA
     9   FILE ANABSTR
     1   FILE ANTE
     1   FILE AQUALINE
    13   FILE AQUASCI
    32   FILE BABS
    42   FILE BIOBUSINESS
    29   FILE BIOCOMMERCE
   108   FILE BIOENG
  2963   FILE BIOSIS
   410   FILE BIOTECHABS
   410   FILE BIOTECHDS
  2012   FILE BIOTECHNO
   231   FILE CABA
  1329   FILE CANCERLIT
```

```
3680   FILE CAPLUS
   7   FILE CASREACT
  26   FILE CBNB
  27   FILE CEABA-VTB
   5   FILE CEN
  20   FILE CIN
  91   FILE COMPENDEX
   1   FILE COMPUAB
  55   FILE CONFSCI
   1   FILE CROPU
   3   FILE DDFB
 147   FILE DDFU
1323   FILE DGENE
 182   FILE DISSABS
  14   FILE DPCI
   3   FILE DRUGB
 190   FILE DRUGU
  27   FILE EMBAL
2637   FILE EMBASE
 212   FILE ENERGY
   1   FILE ENVIROENG
1230   FILE ESBIOBASE
   1   FILE FRFULL
   5   FILE FROSTI
  28   FILE FSTA
 508   FILE GENBANK
   7   FILE HEALSAFE
 278   FILE IFIPAT
   3   FILE IMSDRUGNEWS
 118   FILE INIS
 130   FILE INPADOC
  23   FILE INSPEC
 174   FILE INVESTEXT
  30   FILE IPA
  13   FILE JAPIO
  78   FILE JICST-EPLUS
   2   FILE KOREAPAT
  11   FILE KOSMET
1633   FILE LIFESCI
1989   FILE MEDLINE
   1   FILE NAPRALERT
  12   FILE NIOSHTIC
  69   FILE NLDB
  29   FILE NTIS
   3   FILE OCEAN
 788   FILE PASCAL
   6   FILE PATDPA
  23   FILE PATDPAFULL
2438   FILE PCTFULL
  10   FILE PHARMAML
  24   FILE PHIN
   5   FILE POLLUAB
  79   FILE PROMT
   1   FILE RAPRA
2364   FILE SCISEARCH
   3   FILE TEMA
1139   FILE TOXCENTER
   2   FILE ULIDAT
3959   FILE USPATFULL
 152   FILE USPAT2
   5   FILE VETU
   2   FILE WATER
 182   FILE WPIDS
   3   FILE WPIFV
```

```
            182   FILE WPINDEX
L4             QUE (L2 OR L3) (30A) HUMAN
               ---------
               SEA L4 (15A) (SUGAR OR SUCROSE OR TREHALOSE OR MANNITOL OR LACT
               ---------
                 1   FILE BIOBUSINESS
                12   FILE BIOSIS
                 3   FILE BIOTECHNO
                 2   FILE CABA
                 4   FILE CANCERLIT
                14   FILE CAPLUS
                 2   FILE DDFU
                 2   FILE DRUGU
                 7   FILE EMBASE
                 1   FILE ENERGY
                37   FILE GENBANK
                 1   FILE HEALSAFE
                 1   FILE INIS
                 4   FILE IPA
                 2   FILE LIFESCI
                 4   FILE MEDLINE
                 1   FILE PASCAL
                14   FILE PCTFULL
                 1   FILE POLLUAB
                 2   FILE SCISEARCH
                 3   FILE TOXCENTER
                17   FILE USPATFULL
                 1   FILE USPAT2
                 1   FILE WPIDS
                 1   FILE WPINDEX
L5             QUE L4 (15A) (SUGAR OR SUCROSE OR TREHALOSE OR MANNITOL OR LACT
               ---------
               SEA (2 OR L3) (15A) (SUGAR OR SUCROSE OR TREHALOSE OR MANNITOL
               ---------
                 1   FILE 1MOBILITY
               491   FILE ABI-INFORM
                88   FILE ADISCTI
                43   FILE AEROSPACE
              2759   FILE AGRICOLA
                11   FILE ALUMINIUM
               738   FILE ANABSTR
                91   FILE ANTE
               105   FILE APOLLIT
                99   FILE AQUALINE
               617   FILE AQUASCI
              2934   FILE BABS
                 5   FILE BIBLIODATA
              1357   FILE BIOBUSINESS
                11   FILE BIOCOMMERCE
              2351   FILE BIOENG
             19716   FILE BIOSIS
              8098   FILE BIOTECHABS
              8098   FILE BIOTECHDS
              4807   FILE BIOTECHNO
             22824   FILE CABA
              1645   FILE CANCERLIT
               483   FILE CAOLD
             59926   FILE CAPLUS
              2545   FILE CASREACT
               274   FILE CBNB
               651   FILE CEABA-VTB
                19   FILE CEN
                20   FILE CERAB
               354   FILE CHEMINFORMRX
```

```
  548   FILE CIN
   42   FILE CIVILENG
 1249   FILE COMPENDEX
    5   FILE COMPUAB
    3   FILE COMPUSCIENCE
   70   FILE CONFSCI
    1   FILE COPPERLIT
    1   FILE CORROSION
  160   FILE CROPB
 1303   FILE CROPU
    7   FILE CSNB
 1430   FILE DDFB
 1063   FILE DDFU
    6   FILE DETHERM
18481   FILE DGENE
 1228   FILE DISSABS
  208   FILE DPCI
 1430   FILE DRUGB
 3937   FILE DRUGU
    5   FILE ELCOM
   14   FILE EMA
   80   FILE EMBAL
 8484   FILE EMBASE
 1014   FILE ENERGY
   39   FILE ENTEC
  102   FILE ENVIROENG
 6087   FILE ESBIOBASE
 1228   FILE FOMAD
   18   FILE FRANCEPAT
 1819   FILE FRFULL
  928   FILE FROSTI
11757   FILE FSTA
27998   FILE GENBANK
   20   FILE GEOREF
   27   FILE HEALSAFE
    2   FILE ICONDA
 7506   FILE IFIPAT
    1   FILE IMSDRUGNEWS
    1   FILE INFODATA
  416   FILE INIS
 1771   FILE INPADOC
  262   FILE INSPEC
   68   FILE INSPHYS
 3708   FILE INVESTEXT
  473   FILE IPA
    9   FILE ITRD
 1998   FILE JAPIO
 2852   FILE JICST-EPLUS
  724   FILE KOREAPAT
   18   FILE KOSMET
 4564   FILE LIFESCI
    1   FILE LISA
    2   FILE MATBUS
    3   FILE MATH
    1   FILE MATHDI
    8   FILE MECHENG
11075   FILE MEDLINE
   28   FILE METADEX
   62   FILE NAPRALERT
  152   FILE NIOSHTIC
 1322   FILE NLDB
  313   FILE NTIS
   20   FILE NUTRACEUT
  107   FILE OCEAN
```

```
   628   FILE PAPERCHEM2
  7480   FILE PASCAL
     1   FILE PATDD
    67   FILE PATDPA
  3954   FILE PATDPAFULL
 26308   FILE PCTFULL
    17   FILE PHARMAML
   199   FILE PHIN
    72   FILE PIRA
   131   FILE POLLUAB
  5457   FILE PROMT
    76   FILE RAPRA
 14189   FILE SCISEARCH
     4   FILE SOLIDSTATE
    13   FILE SYNTHLINE
    81   FILE TEMA
    36   FILE TEXTILETECH
  8506   FILE TOXCENTER
    38   FILE TULSA
    27   FILE ULIDAT
 65450   FILE USPATFULL
  3267   FILE USPAT2
    15   FILE VETB
   359   FILE VETU
   211   FILE WATER
     1   FILE WELDASEARCH
 12420   FILE WPIDS
    31   FILE WPIFV
 12420   FILE WPINDEX
    32   FILE WSCA
    26   FILE WTEXTILES
L6        QUE (2 OR L3) (15A) (SUGAR OR SUCROSE OR TREHALOSE OR MANNITOL
          ---------
          SEA L4 AND L6
          ---------
     1   FILE BIOBUSINESS
     7   FILE BIOSIS
     1   FILE BIOTECHABS
     1   FILE BIOTECHDS
     7   FILE BIOTECHNO
     1   FILE CABA
     7   FILE CANCERLIT
    14   FILE CAPLUS
     1   FILE COMPENDEX
     2   FILE DDFU
     2   FILE DISSABS
     2   FILE DRUGU
    10   FILE EMBASE
     3   FILE ENERGY
     2   FILE ESBIOBASE
    46   FILE GENBANK
     2   FILE IFIPAT
     4   FILE INIS
     4   FILE IPA
     5   FILE LIFESCI
     6   FILE MEDLINE
     1   FILE PATDPAFULL
   902   FILE PCTFULL
     7   FILE SCISEARCH
     4   FILE TOXCENTER
  1473   FILE USPATFULL
    33   FILE USPAT2
     1   FILE WPIDS
     1   FILE WPINDEX
```

```
L7              QUE L4 AND L6
                ---------
                SEA L7 AND PY<1995
                ---------
                4    FILE BIOSIS
                5    FILE BIOTECHNO
                1    FILE CABA
                7    FILE CANCERLIT
                9    FILE CAPLUS
                0*   FILE CONFSCI
                2    FILE DISSABS
                7    FILE EMBASE
                3    FILE ENERGY
                0*   FILE FORIS
                4    FILE INIS
                2    FILE LIFESCI
                5    FILE MEDLINE
                1    FILE PATDPAFULL
               34    FILE PCTFULL
                1    FILE SCISEARCH
                4    FILE TOXCENTER
                0*   FILE UFORDAT
               47    FILE USPATFULL
L8              QUE L7 AND PY<1995
                ---------

     FILE 'USPATFULL, PCTFULL, CAPLUS, CANCERLIT, EMBASE, BIOTECHNO, MEDLINE,
     BIOSIS, TOXCENTER, ENERGY, DISSABS, LIFESCI, CABA, PATDPAFULL, SCISEARCH'
     ENTERED AT 12:07:51 ON 06 JAN 2005
L9            83 S L8 AND (LIQUID OR SOLUTION OR SOLUTE OR SUSPENSION OR MIXTURE
L10           82 DUP REM L9 (1 DUPLICATE REMOVED)
```

L1 ANSWER 1 OF 10 REGISTRY COPYRIGHT 2005 ACS on STN
RN 392013-00-2 REGISTRY
ED Entered STN: 13 Feb 2002
CN DNA (human gene LSD cDNA) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 430: PN: WO2004024892 FIGURE: 7 unclaimed DNA
CN DNA (human liver/spleen gene LSD DNase I-like 3 protein cDNA plus flanks)
CN **DNase γ (human liver/spleen gene LSD cDNA plus flanks)**
CN GenBank AF047354
FS NUCLEIC ACID SEQUENCE
MF Unspecified
CI MAN
SR GenBank
LC STN Files: CA, CAPLUS, GENBANK, TOXCENTER, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); PRP (Properties); USES (Uses)

RELATED SEQUENCES AVAILABLE WITH SEQLINK

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L1 ANSWER 2 OF 10 REGISTRY COPYRIGHT 2005 ACS on STN
RN 366521-25-7 REGISTRY
ED Entered STN: 02 Nov 2001
CN Nuclease, deoxyribo- (human N-terminal fragment) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 11: PN: WO0174905 SEQID: 204 claimed protein
CN **DNase I (human)**
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PRP (Properties)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L1 ANSWER 3 OF 10 REGISTRY COPYRIGHT 2005 ACS on STN
RN 326630-22-2 REGISTRY
ED Entered STN: 11 Mar 2001
CN Nuclease, deoxyribo- (human isoenzyme DLAD (DNase II-Like Acid DNase)) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 1: PN: WO0112793 SEQID: 3 claimed protein
CN **DNase DLAD (DNase II-Like Acid DNase) (human)**
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); PRP (Properties); USES (Uses)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L1 ANSWER 4 OF 10 REGISTRY COPYRIGHT 2005 ACS on STN
RN 251309-67-8 REGISTRY
ED Entered STN: 17 Dec 1999
CN Nuclease, exodeoxyribo-, X (9CI) (CA INDEX NAME)
OTHER NAMES:
CN **DNase X**
CN Exonuclease X
MF Unspecified
CI MAN
SR CA
LC STN Files: BIOSIS, CA, CAPLUS, TOXCENTER, USPATFULL
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: BIOL (Biological study); PRP (Properties); USES (Uses)
RL.NP Roles from non-patents: BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
11 REFERENCES IN FILE CA (1907 TO DATE)
11 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L1 ANSWER 5 OF 10 REGISTRY COPYRIGHT 2005 ACS on STN
RN 208939-71-3 REGISTRY
ED Entered STN: 23 Jul 1998
CN Nuclease, endodeoxyribo-, CPAN (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Caspase-activated deoxyribonuclease
CN Caspase-activated DNase
CN Caspase-activated nuclease
CN CPAN (enzyme)
CN DFF40/CAD endonuclease
CN DNA Fragmentation Factor 40
CN DNase CAD
CN DNase CPAN
CN DNase DFF-40
CN **DNase XAD**
MF Unspecified
CI MAN
SR CA
LC STN Files: BIOSIS, CA, CAPLUS, TOXCENTER, USPATFULL
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)
RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); PREP (Preparation); PRP (Properties); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)
RLD.NP Roles for non-specific derivatives from non-patents: BIOL (Biological study); PRP (Properties)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
110 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
111 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L1 ANSWER 6 OF 10 REGISTRY COPYRIGHT 2005 ACS on STN
RN 159913-26-5 REGISTRY
ED Entered STN: 04 Jan 1995
CN Nuclease, endodeoxyribo-, IV (human reduced) (9CI) (CA INDEX NAME)

OTHER NAMES:
CN 10: PN: WO0036109 SEQID: 10 unclaimed protein
CN 112: PN: US5994069 SEQID: 137 unclaimed protein
CN 71: PN: US5985557 FIGURE: 70 unclaimed sequence
CN **DNase IV (human)**
CN Endodeoxyribonuclease (human gene FEN-1)
CN Flap endonuclease (human gene FEN-1)
CN Nuclease, deoxyribonucleate flap structure endodeoxyribo-, FEN-1 (human)
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: BIOL (Biological study); PRP (Properties); USES (Uses)
RL.NP Roles from non-patents: BIOL (Biological study); OCCU (Occurrence); PROC (Process); PRP (Properties)

RELATED SEQUENCES AVAILABLE WITH SEQLINK

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
7 REFERENCES IN FILE CA (1907 TO DATE)
7 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L1 ANSWER 7 OF 10 REGISTRY COPYRIGHT 2005 ACS on STN
RN 63363-78-0 REGISTRY
ED Entered STN: 16 Nov 1984
CN Nuclease, endodeoxyribo-, IV (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 5'-Apurinic-apyrimidinic endonuclease Apn1
CN AP endonuclease IV
CN AP endonuclease type IV
CN Apurinic/apyrimidinic endonuclease type IV
CN DNA endonuclease IV
CN **DNase IV**
CN E.C. 3.1.21.2
CN Endonuclease IV
CN Type IV AP endonuclease
CN Type IV apurinic/apyrimidinic endonuclease
MF Unspecified
CI MAN
LC STN Files: AGRICOLA, BIOBUSINESS, BIOSIS, CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL
DT.CA CAplus document type: Conference; Dissertation; Journal; Patent
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PRP (Properties); USES (Uses)
RLD.P Roles for non-specific derivatives from patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PRP (Properties); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RLD.NP Roles for non-specific derivatives from non-patents: BIOL (Biological study); PRP (Properties)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
156 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
157 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L1 ANSWER 8 OF 10 REGISTRY COPYRIGHT 2005 ACS on STN

RN 61970-03-4 REGISTRY
ED Entered STN: 16 Nov 1984
CN Nuclease, endodeoxyribo-, V (9CI) (CA INDEX NAME)
OTHER NAMES:
CN **DNase V**
CN E.C. 3.1.22.3
CN Endodeoxyribonuclease V
CN Endonuclease V
CN Escherichia coli Endodeoxyribonuclease V
MF Unspecified
CI MAN
LC STN Files: AGRICOLA, BIOSIS, CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL
DT.CA CAplus document type: Conference; Dissertation; Journal; Patent; Report
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PRP (Properties); USES (Uses)
RLD.P Roles for non-specific derivatives from patents: ANST (Analytical study); BIOL (Biological study); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)
RLD.NP Roles for non-specific derivatives from non-patents: BIOL (Biological study); PROC (Process); PRP (Properties)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
141 REFERENCES IN FILE CA (1907 TO DATE)
6 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
141 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L1 ANSWER 9 OF 10 REGISTRY COPYRIGHT 2005 ACS on STN
RN 61461-51-6 REGISTRY
ED Entered STN: 16 Nov 1984
CN Nuclease, endodeoxyribo-, VI (9CI) (CA INDEX NAME)
OTHER NAMES:
CN **DNase VI**
MF Unspecified
CI MAN
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL
DT.CA CAplus document type: Conference; Journal; Patent
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); USES (Uses)
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
6 REFERENCES IN FILE CA (1907 TO DATE)
6 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L1 ANSWER 10 OF 10 REGISTRY COPYRIGHT 2005 ACS on STN
RN 9003-98-9 REGISTRY
ED Entered STN: 16 Nov 1984
CN Nuclease, deoxyribo- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Alkaline deoxyribonuclease
CN Alkaline DNase
CN Deoxyribonuclease
CN Deoxyribonuclease (pancreatic)
CN Deoxyribonuclease A
CN Deoxyribonuclease I
CN Deoxyribonucleic phosphatase
CN Desoxyribonuclease
CN DNA depolymerase
CN DNA endonuclease
CN DNA nuclease
CN DNAase
CN **DNase**

CN DNase γ
CN **DNase I**
CN **DNase Y**
CN Dornase
CN Dornava
CN Dornavac
CN E.C. 3.1.21.1
CN E.C. 3.1.4.5
CN Endodeoxyribonuclease I
CN Endonuclease DNAS1L3
CN Endonuclease S
CN Escherichia coli Endonuclease I
CN NUC18 nuclease
CN Nuclease, Escherichia coli endo-, I
CN Pancreatic deoxyribonuclease
CN Pancreatic dornase
DR 9002-00-0, 9036-35-5, 9037-43-8, 9037-64-3, 9038-13-5
MF Unspecified
CI COM, MAN
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DIOGENES, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IMSPATENTS, IMSRESEARCH, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, PHAR, PIRA, PROMT, RTECS*, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)
DT.CA CAplus document type: Book; Conference; Dissertation; Journal; Patent; Report
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)
RLD.P Roles for non-specific derivatives from patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)
RLD.NP Roles for non-specific derivatives from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
7431 REFERENCES IN FILE CA (1907 TO DATE)
118 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
7440 REFERENCES IN FILE CAPLUS (1907 TO DATE)

Inventor Search

=> d ibib abs ind l5 1-2

L5 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:345888 HCAPLUS
DOCUMENT NUMBER: 136:321284
TITLE: Improved stability of DNase in pharmaceutical solutions using Ca2+ and sugars
INVENTOR(S): **Chan, Hak-Kim; Gonda, Igor; Shire, Steven J.; Weck, Suzanne Sin-Mui Lo**
PATENT ASSIGNEE(S): Genentech, Inc., USA
SOURCE: U.S., 19 pp., Cont.-in-part of U.S. Ser. No. 377,527, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6383788	B1	20020507	US 1996-696955	19961203
WO 9523854	A1	19950908	WO 1995-US2457	19950228
W: CA, JP, US, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 2003054532	A1	20030320	US 2002-76213	20020212

PRIORITY APPLN. INFO.:

US 1994-206504	B1	19940304
US 1995-377527	B2	19950120
WO 1995-US2457	W	19950228
US 1996-696955	A1	19961203

AB The present invention relates to the use of calcium ion and/or sugars to minimize thermal aggregation of DNase and to the use of calcium ion to stabilize liquid solns. of DNase under acidic pH conditions. DNase is the active pharmaceutical principle and the solns. may contain other pharmaceutically acceptable excipients making them suitable for pharmaceutical administration. It was previously shown that DNase undergoes deamidation in acidic solns and may not be suitable for use in pharmaceutical compns. In the first instance, calcium ion/sugar minimizes the effects of thermal aggregation in the solution In the second aspect, calcium ion stabilizes the lower pH solns. from protein precipitation Concns. of 1 mM to 1 M of calcium chloride, calcium oxide or calcium carbonate may be used to improve the stability of DNase in solution wherein the temperature may be elevated above 60°C. Sugars include α-lactose monohydrate, trehalose, mannitol and sucrose at concns. of 50-200 mg/mL. In a preferred embodiment, a 10-100 mM concentration of calcium chloride is used to improve DNase stability. Temps. may be elevated in the spray-drying process for collection of a respirable DNase powder that is therapeutically effective in treatment of lung diseases.

IC ICM C12N009-96
ICS C12N009-16
NCL 435188000
CC 7-2 (Enzymes)
Section cross-reference(s): 1, 63
ST stability DNase soln calcium ion sugar; DNase thermal stability drug delivery systems; aggregation acid pH DNase stability
IT Lung
(DNase for improved mucus viscosity in; improved stability of DNase in pharmaceutical solns. using Ca2+ and sugars)

IT Bos taurus
Human
(DNase of; improved stability of DNase in pharmaceutical solns. using Ca2+ and sugars)
IT Carbohydrates, biological studies
Monosaccharides
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(DNase solution stability improved by; improved stability of DNase in pharmaceutical solns. using Ca2+ and sugars)
IT pH
(DNase with improved stability in solns. of acidic; improved stability of DNase in pharmaceutical solns. using Ca2+ and sugars)
IT Solutions
(DNase; improved stability of DNase in pharmaceutical solns. using Ca2+ and sugars)
IT Temperature effects, biological
(for aggregation of DNase in solution; improved stability of DNase in pharmaceutical solns. using Ca2+ and sugars)
IT Drug delivery systems
(inhalants, DNase as; improved stability of DNase in pharmaceutical solns. using Ca2+ and sugars)
IT Drug delivery systems
(liqs., DNase as; improved stability of DNase in pharmaceutical solns. using Ca2+ and sugars)
IT Aggregation
(prevention of DNase; improved stability of DNase in pharmaceutical solns. using Ca2+ and sugars)
IT Amidation
(retro, inhibition of DNase; improved stability of DNase in pharmaceutical solns. using Ca2+ and sugars)
IT Lung
(toxicity, DNase for improved mucus viscosity in; improved stability of DNase in pharmaceutical solns. using Ca2+ and sugars)
IT Spray atomizers
(ultrasonic, DNase formulation for; improved stability of DNase in pharmaceutical solns. using Ca2+ and sugars)
IT 471-34-1, Calcium carbonate, biological studies 1305-78-8, Calcium oxide, biological studies 10043-52-4, Calcium chloride, biological studies 14127-61-8, Ca2+, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(DNase with improved stability in solns. of acidic pH using; improved stability of DNase in pharmaceutical solns. using Ca2+ and sugars)
IT 57-50-1, Sucrose, biological studies 69-65-8, Mannitol 99-20-7, Trehalose 5989-81-1, α-Lactose monohydrate
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(DNase with improved stability using; improved stability of DNase in pharmaceutical solns. using Ca2+ and sugars)
IT 9003-98-9, DNase
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(improved stability of DNase in pharmaceutical solns. using Ca2+ and sugars)
REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:890317 HCAPLUS

DOCUMENT NUMBER: 123:296642
TITLE: Improved DNase liquid solutions using calcium and sugars to enhance storage stability
INVENTOR(S): **Chan, Hak-Kim; Gonda, Igor; Shire, Steven J.; Weck, Suzanne Sin-mui Lo**
PATENT ASSIGNEE(S): Genentech, Inc., USA
SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9523854	A1	19950908	WO 1995-US2457	19950228
W: CA, JP, US, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2184581	AA	19950908	CA 1995-2184581	19950228
EP 748377	A1	19961218	EP 1995-911123	19950228
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 09503394	T2	19970408	JP 1995-522968	19950228
JP 3009224	B2	20000214		
US 6383788	B1	20020507	US 1996-696955	19961203
US 2003054532	A1	20030320	US 2002-76213	20020212

PRIORITY APPLN. INFO.:

US 1994-206504	A	19940304
US 1995-377527	A	19950120
WO 1995-US2457	W	19950228
US 1996-696955	A1	19961203

AB The present invention relates to the use of calcium ion and/or sugars to minimize thermal aggregation of DNase and to the use of calcium ion to stabilize liquid solns. of DNase, the solns. having a pH of less than neutral. DNase is the active pharmaceutical principle and the solns. may contain other pharmaceutically acceptable excipients making them suitable for pharmaceutical administration. In the first instance, calcium ion/sugar minimizes the effects of thermal aggregation in the solution In the second aspect, calcium ion stabilizes the lower pH solns. from protein precipitation

IC ICM C12N009-96
ICS A61K038-46; A61K009-12
CC 63-6 (Pharmaceuticals)
ST DNase liq pharmaceutical stability calcium sugar
IT Monosaccharides
RL: NUU (Other use, unclassified); USES (Uses)
(improved DNase liquid solns. using calcium and sugars to enhance storage stability)
IT Pharmaceutical dosage forms
(inhalants, improved DNase liquid solns. using calcium and sugars to enhance storage stability)
IT Pharmaceutical dosage forms
(liqs., improved DNase liquid solns. using calcium and sugars to enhance storage stability)
IT 57-50-1, Sucrose, uses 69-65-8, Mannitol 99-20-7, Trehalose 5989-81-1, α-Lactose monohydrate 7440-70-2, Calcium, uses 10043-52-4, Calcium chloride, uses
RL: NUU (Other use, unclassified); USES (Uses)
(improved DNase liquid solns. using calcium and sugars to enhance storage stability)
IT 9003-98-9, Deoxyribonuclease

RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(improved DNase liquid solns. using calcium and sugars to enhance storage stability)

```
=> d que stat l17
L7             1 SEA FILE=REGISTRY ABB=ON  DNASE/CN
L8             1 SEA FILE=REGISTRY ABB=ON  PHOSPHODIESTERASE/CN
L9         45218 SEA FILE=HCAPLUS ABB=ON  L7 OR L8 OR ?DNASE? OR ?PHOSPHODIESTER
                 ASE?
L10          473 SEA FILE=HCAPLUS ABB=ON  L9 AND (?POLYDEOXYRIBONUCLEIC?(W)?ACID
                 ? OR ?MONOSACCH? OR ?CARBOHYDRAT?)
L11          103 SEA FILE=HCAPLUS ABB=ON  L10 AND ?HUMAN?
L12           30 SEA FILE=HCAPLUS ABB=ON  L11 AND (?THERM? OR ?HEAT? OR ?TEMP?)
L13           15 SEA FILE=HCAPLUS ABB=ON  L12 AND (?STABLE? OR ?MINIMIZ? OR
                 ?PRECIP? OR ?CLEAR?)
L14           30 SEA FILE=HCAPLUS ABB=ON  L12 OR L13
L17           13 SEA FILE=HCAPLUS ABB=ON  L14 AND (PRD<19961203 OR PD<19961203)

=> d ibib abs l17 1-13

L17  ANSWER 1 OF 13  HCAPLUS  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:         2002:345888  HCAPLUS
DOCUMENT NUMBER:          136:321284
TITLE:                    Improved stability of DNase in
                          pharmaceutical solutions using Ca2+ and sugars
INVENTOR(S):              Chan, Hak-Kim; Gonda, Igor; Shire, Steven J.; Weck,
                          Suzanne Sin-Mui Lo
PATENT ASSIGNEE(S):       Genentech, Inc., USA
SOURCE:                   U.S., 19 pp., Cont.-in-part of U.S. Ser. No. 377,527,
                          abandoned.
                          CODEN: USXXAM
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   2
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     ---------------      ----   --------    --------------------    --------
     US 6383788            B1    20020507    US 1996-696955          19961203 <--
     WO 9523854            A1    19950908    WO 1995-US2457          19950228 <--
         W:  CA, JP, US, US
         RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
     US 2003054532         A1    20030320    US 2002-76213           20020212 <--
PRIORITY APPLN. INFO.:                       US 1994-206504      B1 19940304 <--
                                             US 1995-377527      B2 19950120 <--
                                             WO 1995-US2457      W  19950228 <--
                                             US 1996-696955      A1 19961203
```

AB The present invention relates to the use of calcium ion and/or sugars to **minimize thermal** aggregation of **DNase** and to the use of calcium ion to stabilize liquid solns. of **DNase** under acidic pH conditions. **DNase** is the active pharmaceutical principle and the solns. may contain other pharmaceutically acceptable excipients making them suitable for pharmaceutical administration. It was previously shown that **DNase** undergoes deamidation in acidic solns and may not be suitable for use in pharmaceutical compns. In the first instance, calcium ion/sugar **minimizes** the effects of **thermal** aggregation in the solution In the second aspect, calcium ion stabilizes the lower pH solns. from protein **precipitation** Concns. of 1 mM to 1 M of calcium chloride, calcium oxide or calcium carbonate may be used to improve the stability of **DNase** in solution wherein the **temperature** may be elevated above 60°C. Sugars include α-lactose monohydrate, trehalose, mannitol and sucrose at concns. of 50-200 mg/mL. In a preferred embodiment, a 10-100 mM concentration of calcium

chloride is used to improve **DNase** stability. **Temps.** may be elevated in the spray-drying process for collection of a respirable **DNase** powder that is therapeutically effective in treatment of lung diseases.

REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 2 OF 13 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1996:292998 HCAPLUS
DOCUMENT NUMBER: 124:336009
TITLE: Effects of additives on **heat** denaturation of **rhDNase** in solutions
AUTHOR(S): Chan, Hak-Kim; Au-Yeung, Kwok-Leung; Gonda, Igor
CORPORATE SOURCE: Department Pharmaceutical Research and Development, Genentech, Inc., South San Francisco, CA, 94080, USA
SOURCE: Pharmaceutical Research (**1996**), 13(5), 756-761
CODEN: PHREEB; ISSN: 0724-8741
PUBLISHER: Plenum
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Purpose. to study the **thermal** stability of recombinant **human DNase** I (**rhDNase**) in aqueous solns. Methods. differential scanning calorimetry (DSC) was used to measure the denaturation or melting **temperature** (Tm) and enthalpy (Hm) of **rhDNase.** The effects of denaturants (guanidine HCl and urea) and additives (mainly divalent cations and disaccharides) were investigated at pH 6-7. Results. the Tm and Hm of **rhDNase** in pure water were measured as 67.4° and 18.0 J/g resp., values typical of globular proteins. The melting peak disappeared on re-running the sample after cooling to room **temperature**, indicating that the **thermal** denaturation was irreversible. The latter was due to the occurrence of aggregation accompanying the unfolding process of **rhDNase.** Size exclusion chromatog. indicated that during **heat** denaturation, **rhDNase** formed soluble high mol. weight aggregates with a mol. size >300 kDa estimated by the void volume Of particular interest are the divalent cations: Ca2+ stabilizes **rhDNase** against **thermal** denaturation and elevates Tm and Hm while Mg2+, Mn2+ and Zn2+ destabilize it. Sugars also stabilize **rhDNase.** As expected, denaturants destabilize the protein and lower the Tm and Hm. All destabilization of **rhDNase** can be prevented by adding Ca2+ to the solns. Conclusions. CaCl2 and sugars were found to stabilize **rhDNase** against **thermal** denaturation while divalent cations, urea and guanidine HCl destabilize the protein. The effects could be explained by a mixture of mechanisms. For Ca2+ the protective effect is believed to be due to an ordering of the **rhDNase** structure in its native state, and by prevention of breaking of a disulfide bridge, thus making it less susceptible to unfold under **thermal** stress.

L17 ANSWER 3 OF 13 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1993:187374 HCAPLUS
DOCUMENT NUMBER: 118:187374
TITLE: Method using two-component additive for stabilization of biomaterials during lyophilization
INVENTOR(S): Carpenter, John F.
PATENT ASSIGNEE(S): Cryolife, Inc., USA
SOURCE: PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE	
WO 9300807	A1	19930121	WO 1992-US5643		19920702	<--
W: AT, AU, BB, BG, BR, CA, CH, CS, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO						
AU 9223096	A1	19930211	AU 1992-23096		19920702	<--
PRIORITY APPLN. INFO.:			US 1991-725593	A	19910703	<--
			WO 1992-US5643	A	19920702	<--

AB A method for stabilizing biomaterials during lyophilization uses a two-component additive. The 1st component (PEG, dextran, ficoll, etc.) serves as a cryoprotectant, and the 2nd component (e.g. a sugar polyhydroxy alc., amino acid) protects the biomaterial (e.g. a protein) during drying. In freeze-drying lactate dehydrogenase M isoenzyme with PEG and a second component (trehalose, lactose, glucose, glycine, or mannitol), the results supported synergistic stabilization of the protein during freeze-drying.

L17 ANSWER 4 OF 13 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1984:188438 HCAPLUS
DOCUMENT NUMBER: 100:188438
TITLE: Modified labeled nucleotides and polynucleotides and methods of utilizing and detecting them
INVENTOR(S): Engelhardt, Dean; Rabbani, Elazar; Kline, Stanley; Stavrianopoulos, Jannis G.; Kirtikar, Dollie
PATENT ASSIGNEE(S): Enzo Biochem, Inc., USA
SOURCE: Eur. Pat. Appl., 140 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
EP 97373	A2	19840104	EP 1983-106112	19830622	<--
EP 97373	A3	19840606			
EP 97373	B1	19921007			
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE					
CA 1223831	A1	19870707	CA 1983-430882	19830621	<--
ES 523503	A1	19860916	ES 1983-523503	19830622	<--
IL 69051	A1	19880229	IL 1983-69051	19830622	<--
EP 285057	A2	19881005	EP 1988-104961	19830622	<--
EP 285057	A3	19901031			
EP 285057	B1	19950301			
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE					
EP 285058	A2	19881005	EP 1988-104962	19830622	<--
EP 285058	A3	19900926			
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE					
EP 285950	A2	19881012	EP 1988-104964	19830622	<--
EP 285950	A3	19901107			
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE					
EP 286898	A2	19881019	EP 1988-104963	19830622	<--
EP 286898	A3	19900808			
EP 286898	B1	19980429			
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE					
EP 302175	A2	19890208	EP 1988-104965	19830622	<--
EP 302175	A3	19901031			

R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE					
AT 81342	E	19921015	AT 1983-106112	19830622	<--
EP 618228	A1	19941005	EP 1994-105993	19830622	<--
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE					
AT 165605	E	19980515	AT 1988-104963	19830622	<--
DK 8302911	A	19831224	DK 1983-2911	19830623	<--
NO 8302292	A	19831227	NO 1983-2292	19830623	<--
AU 8316179	A1	19840105	AU 1983-16179	19830623	<--
AU 585199	B2	19890615			
JP 59062600	A2	19840410	JP 1983-113599	19830623	<--
JP 11292892	A2	19991026	JP 1999-8415	19830623	<--
DK 8401306	A	19840229	DK 1984-1306	19840229	<--
DK 8401307	A	19840229	DK 1984-1307	19840229	<--
ES 539316	A1	19861001	ES 1985-539316	19850102	<--
ES 547320	A1	19860316	ES 1985-547320	19850926	<--
ES 547319	A1	19880416	ES 1985-547319	19850926	<--
AU 8941493	A1	19900104	AU 1989-41493	19890915	<--
US 5241060	A	19930831	US 1990-532704	19900604	<--
US 5260433	A	19931109	US 1990-567039	19900813	<--
JP 06234787	A2	19940823	JP 1993-177184	19930610	<--
JP 2760466	B2	19980528			
JP 10158294	A2	19980616	JP 1997-295889	19971028	<--
JP 3170235	B2	20010528			

PRIORITY APPLN. INFO.:	US 1982-391440	A	19820623 <--
	EP 1983-106112	P	19830622 <--
	EP 1988-104961	A3	19830622 <--
	DK 1983-2911	A	19830623 <--
	JP 1993-177184	A3	19830623 <--
	JP 1997-295889	A3	19830623 <--
	US 1984-674352	B1	19841121 <--
	US 1988-140980	B3	19880105 <--

AB Nucleotides, polynucleotides, and DNA were chemical modified or labeled with chemical moieties which were readily detectable. These chemical moieties included **carbohydrates** and sugars, electron dense substances, magnetic substances, enzymes, coenzymes, hormones, radioactive substances, metals, fluorescent substances, antigens, or antibodies. These chemical modified nucleotides were used for: (1) stimulating or inducing cells to produce lymphokines, cytokinins, and interferon; (2) testing resistance of bacteria to antibiotics; (3) diagnosing genetic disorders, e.g., β-thalassemia; (4) diagnosing tumors; (5) diagnosing bacteria, virus, or fungus infection; and (6) karyotyping chromosomes.

L17 ANSWER 5 OF 13 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:	1983:535756 HCAPLUS
DOCUMENT NUMBER:	99:135756
TITLE:	Comparative physicochemical and immunochemical study of three soluble antigens of **human** leukocytes
AUTHOR(S):	Petrunin, D. D.; Lopukhin, Yu. M.; Shevchenko, O. P.
CORPORATE SOURCE:	N. I. Pirogov Moscow Med. Inst., Moscow, USSR
SOURCE:	Byulleten Eksperimental'noi Biologii i Meditsiny (**1983**), 96(7), 72-4 CODEN: BEBMAE; ISSN: 0365-9615
DOCUMENT TYPE:	Journal
LANGUAGE:	Russian

AB Three soluble leukocytic antigens SLA3, SLA4, and SLA5 were extracted from **human** peripheral leukocytes after freezing and thawing, the antigens were quantitated by **immunopptn.** with monospecific antibodies. SLA3 was a 35-kilodalton (kDa), **heat**- and papain-sensitive β1-glycoprotein; SLA4 is a 80-kDa, **heat**-,

papain-, and trypsin-sensitive β1-glycoprotein; and SLA5 is a 40-kDa **heat**-, papain-, and trypsin-resistant α2-glycoprotein. The antigens were resistant to **DNase**, RNase, and hyaluronidase, did not contain sialic acid, and were **precipitated** with TCA, sulfosalicylic acid, and 30-60%-saturated (NH4)2SO4; this indicates their globin character, and relatively low content of **carbohydrates.** All 3 antigens were present in pus, spleen, and lymph nodes. SLA3 and SLA4 were found in the kidney, SLA4 was present in the lung, and SLA3 was detected in milk, saliva, and amniotic fluid.

L17 ANSWER 6 OF 13 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1983:436913 HCAPLUS
DOCUMENT NUMBER: 99:36913
TITLE: Characterization of Toxoplasma gondii antigens that react with **human** immunoglobulin M and immunoglobulin G antibodies
AUTHOR(S): Naot, Yehudith; Guptill, Douglas R.; Mullenax, Jean; Remington, Jack S.
CORPORATE SOURCE: Dep. Immunol. Infect. Dis., Palo Alto Med. Found., Palo Alto, CA, 94301, USA
SOURCE: Infection and Immunity (**1983**), 41(1), 331-8
CODEN: INFIBR; ISSN: 0019-9567
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Studies were performed to define the nature of the T. gondii antigens that are recognized by **human** IgM and IgG. Both IgM and IgG were directed mainly against T. gondii membrane antigens in sera obtained from patients with acute toxoplasmosis. Treatment of the membrane preparation with **DNase**, RNase, or lipase had no apparent effect on the reactivity of the membrane antigens with IGM and IgG. Lipids isolated from tachyzoites were not recognized by either IgM or IgG. Exposure of T. gondii membranes to **heat**, proteolysis, or oxidation with NaIO4 decreased the reactivity of the membrane prepns. with both IgM and IgG. A preparation of T. gondii proteins and polysaccharides were recognized by both Ig classes. T. gondii Polysaccharides reacted with **human** IgG produced during both the acute and chronic phases of the infection. Apparently, after infection with T. gondii, IgM and IgG antibodies are elicited in response to both protein and **carbohydrate** constituents of the invading parasite.

L17 ANSWER 7 OF 13 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1981:527049 HCAPLUS
DOCUMENT NUMBER: 95:127049
TITLE: Purification and characterization of **heat** -labile enterotoxin produced by ENT+ Escherichia coli: application of hydrophobic chromatography and use of defined media
AUTHOR(S): Robertson, Donald C.; Kunkel, Steven L.; Gilligan, Peter H.
CORPORATE SOURCE: Dep. Microbiol., Univ. Kansas, Lawrence, KS, 66045, USA
SOURCE: Symp. Cholera, Proc. Jt. Conf., U.S.-Jpn. Coop. Med. Sci. Program, Cholera Panel, 14th (**1979**), Meeting Date 1978, 250-65. Editor(s): Takeya, Kenji; Zinnaka, Yutaka. U.S.-Jap. Cooperative Med. Sci. Program, Japanese Cholera Panel: Tokyo, Japan.
CODEN: 46CDAD
DOCUMENT TYPE: Conference
LANGUAGE: English
AB **Heat**-labile enterotoxin (LT) produced by a **human**

strain of ENT+ E. coli (286C2) was purified to homogeneity by ultrafiltration, (NH4)2SO4 fractionation, hydrophobic chromatog. on norleucine-Sepharose, hydroxylapatite chromatog., and Bio-Gel P-150 gel filtration. Optimal yields of cell-associated LT were obtained by suspending cells grown using a defined medium in 0.12M Tris Cl, pH 8.5. The overall yield of LT was 20% and represented about a 500-fold purification over the pH extract Purified LT had a mol. weight of 73,000 daltons, which dissociated in neutral SDS at room **temperature** into fragments of 44,000 and 30,000 daltons as monitored by SDS-gel electrophoresis. Purified LT prepns. were remarkably **stable** over a wide range of storage conditions, **temps.**, and pHs. The biol. activity was increased by incubation with trypsin and completely destroyed by pronase and proteinase K; whereas, **DNase** I, RNase, and phospholipase D had no effect. The amino acid composition of purified LT was quite different from cholera toxin and neither **carbohydrate** nor LPS was present in purified prepns. Ouchterlony anal. indicated that LT and cholera toxin have ≥1 antigenic determinant in common and each has a min. of 1 unique antigenic determinant. Antiserum raised against 286C2 LT more effectively neutralized cholera toxin than anticholeragenoid neutralized LT. The purification appears applicable to LT produced by other **human** and porcine strains but with reduced yields since most strains do not synthesize as much enterotoxin as 286C2. The data shows that LT and cholera toxin share many common chemical and phys. properties but must be purified by different techniques.

L17 ANSWER 8 OF 13 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1980:213365 HCAPLUS
DOCUMENT NUMBER: 92:213365
TITLE: Isolation and characterization of a **human** liver and kidney-specific protein: the hepato-renal (H-R) antigen
AUTHOR(S): Nerenberg, S. T.; Prasad, R.; Inboriboon, P.; Biskup, N.; Pedersen, L.; Faiferman, I.
CORPORATE SOURCE: Med. Sch., Univ. Illinois, Chicago, IL, 60612, USA
SOURCE: Clinical and Experimental Immunology (**1980**), 39(3), 626-34
CODEN: CEXIAL; ISSN: 0009-9104
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The isolation and characterization is described of a soluble antigen shared by the liver and kidney of **human** and some other animal species. Homogenates of **human** liver in saline were centrifuged at 27,000 g and the supernatants were fractionated by preparative polyacrylamide gel electrophoresis. The gels were divided in sections and each was injected into rabbits; after absorption with polymerized normal **human** serum, the antiserum obtained by injecting 1 of the sections reacted only with saline exts. of **human** liver and kidney when tested against a variety of **human** tissue exts. The absorbed antiserum, polymerized and insolubilized with glutaraldehyde, was used to purify the antigen by affinity chromatog. The purified antigen was a glycoprotein containing 19% **carbohydrate**, had a mol. weight of 5.8-6.0 + 104 daltons and a pI of 7.2-7.4. The antigen, relatively **thermostable**, was **precipitated** by 35-55% (NH4)2SO4; its antigenic activity was not affected by extraction with 0.6N perchloric acid or by incubation with RNase, **DNase**, or neuraminidase but was destroyed by incubation with trypsin or chymotrypsin. Immunoperoxidase studies showed that the antigen appeared concentrated in the nuclei of liver and kidney glomerular epithelial and tubular epithelial cells in **humans** and rats. The antigen could not be detected in **human** hepatomas or hypernephromas or in the rat Morris hepatoma 5123.

L17 ANSWER 9 OF 13 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1980:106132 HCAPLUS
DOCUMENT NUMBER: 92:106132
TITLE: Isolation and characterization of a **human** pancreas-specific protein
AUTHOR(S): Nerenberg, Samuel T.; Prasad, Rameshwar; DeMarco Pedersen, Linda; Biskup, Nancy S.; Faiferman, I.
CORPORATE SOURCE: Dep. Pathol., Univ. Illinois Med. Cent, Chicago, IL, 60612, USA
SOURCE: Clinical Chemistry (Washington, DC, United States) (**1980**), 26(2), 209-13
CODEN: CLCHAU; ISSN: 0009-9147
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Homogenates of **human** pancreas in saline were centrifuged at 27,000 g and the supernates were fractionated by preparative polyacrylamide gel electrophoresis. The gels were divided into sections and each section was injected into rabbits; after absorption with polymerized serum from apparently normal **humans**, the antiserum obtained by injecting 1 of the sections was tested against a variety of **human** tissue exts. but reacted only with saline exts. of **human** pancreas. The absorbed antiserum, polymerized and made insol. with glutaraldehyde, was used to purify a pancreas-specific antigen by immunoaffinity batch technique. The purified antigen was a protein with some **carbohydrate** content (180 mg/g by weight) and a mol. weight of .apprx.2.25 + 105 daltons. The antigen was relatively **thermostable** and **precipitated** in the range of 245.64-340.2 g/L saturated (NH4)2SO4; its antigenic activity was not affected by incubation with RNase or **DNase**, but was destroyed by incubation with trypsin or neuraminidase and by extraction with HClO4. Immunofluorescence studies showed that the antigen is diffusely present in the cytoplasm of pancreatic acinar cells. This pancreatic-specific antigen, leached into the circulation, may be of value in diagnosis of subclin. pancreatitis.

L17 ANSWER 10 OF 13 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1979:535863 HCAPLUS
DOCUMENT NUMBER: 91:135863
TITLE: Purification and chemical characterization of the **heat**-labile enterotoxin produced by enterotoxigenic Escherichia coli
AUTHOR(S): Kunkel, Steven L.; Robertson, Donald C.
CORPORATE SOURCE: Dep. Microbiol., Univ. Kansas, Lawrence, KS, 66045, USA
SOURCE: Infection and Immunity (**1979**), 25(2), 586-96
CODEN: INFIBR; ISSN: 0019-9567
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Heat**-labile enterotoxin (LT) produced by a **human** strain of enterotoxigenic E. coli (286C2) was purified to homogeneity from pH exts. of fermentor-grown cells by ultrafiltration, (NH4)2SO4 fractionation, hydrophobic chromatog. on norleucine-Sepharose 4B, hydroxylapatite chromatog., and Bio-Gel P-150 filtration. Purified LT prepns. exhibited biol. activity comparable to that of cholera toxin in 4 bioassays specific for the 2 enterotoxins. The overall yield of LT protein was 20%, which represented a 500-fold purification over pH exts. A native mol. weight of 73,000 was determined by gel electrophoresis. The toxin dissociated upon treatment with Na dodecyl sulfate, pH 7.0, into 2 components with mol. wts. of 44,000 and 30,000. Purified LT prepns. were remarkably **stable** over a wide range of storage conditions, **temps.**,

and pH's. The biol. activity was increased by incubation with trypsin and completely destroyed by Pronase and proteinase K, whereas **DNase** I, RNase, and phospholipase D had no effect. The amino acid composition of purified LT was quite different from that of cholera toxin. Neither **carbohydrate** nor lipopolysaccharide was present in purified prepns. The purification scheme appeared applicable to LT produced by other **human** and porcine enterotoxigenic strains, but reflected the amount of LT produced by each strain. Thus, LT and cholera toxin share many common chemical and phys. properties., but must be purified by different techniques.

L17 ANSWER 11 OF 13 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1978:595257 HCAPLUS
DOCUMENT NUMBER: 89:195257
TITLE: Group A streptococcal membranes: isolation and immunochemical studies
AUTHOR(S): Van de Rijn, Ivo; Zabriskie, John B.
CORPORATE SOURCE: Rockefeller Univ., New York, NY, USA
SOURCE: Biol. Chem. Basement Membr., [Proc. Int. Symp.], 1st (**1978**), Meeting Date 1976, 589-600. Editor(s): Kefalides, Nicholas A. Academic: New York, N. Y. CODEN: 39ISAU
DOCUMENT TYPE: Conference
LANGUAGE: English
AB Components of membranes from group A streptococci are cross-reactive with various tissue antigens: i.e., sarcolemmal **sheath** of myocardium, caudate nucleus, and glomerular basement membranes. Group A streptococci were harvested in the logarithmic phase of growth, and the cell wall was removed under osmotically stabilized conditions using purified group C streptococcal phage-associated lysin. After removal of the solubilized wall polymers, the protoplasts were lyzed and treated with **DNase** and RNase followed by extensive washings in phosphate buffered saline. The purified protoplast membrane contained 74% protein, 2.5% **carbohydrate**, the remainder of which was lipid. On Na dodecyl sulfate slab gel acrylamide electrophoresis, the protein fraction of the protoplast membrane showed 35 major and 10 minor polypeptides. A fraction containing 4 polypeptides has been isolated which is cross-reactive with **human** sarcolemmal **sheath** from myocardium and removes heart-reactive antibody from the serums of acute rheumatic fever patients. This cross-reactive antigen is not involved with the caudate nucleus or glomerular basement membrane cross-reacting systems.

L17 ANSWER 12 OF 13 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1972:402446 HCAPLUS
DOCUMENT NUMBER: 77:2446
TITLE: Determination of the tryptophan content of proteins by ion exchange chromatography of alkaline hydrolysates
AUTHOR(S): Hugli, Tony E.; Moore, Stanford
CORPORATE SOURCE: Rockefeller Univ., New York, NY, USA
SOURCE: Journal of Biological Chemistry (**1972**), 247(9), 2828-34
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A study of the variables in techniques for alkaline hydrolysis of proteins and for chromatog. anal. of the products has led to a method for the accurate determination of tryptophan. Quant. recoveries of tryptophan are obtained when proteins (1-5 mg) are hydrolyzed at 110° or 135° in 0.6 ml of 4.2N NaOH containing 25 mg of starch. Ion exchange chromatography of tryptophan on Beckman PA-35 resin (column height 8 or 12 cm) was

accomplished in 30-50 min with pH 5.4 buffer, 0.21N in Na+. Integral values (100 ± 3%) were obtained for the expected number of tryptophan residues in tryptophyl-leucine, **human** serum albumin, porcine pepsin, sperm whale apomyoglobin, and in bovine α-chymotrypsin, trypsin, **DNase**, and serum albumin. Since **carbohydrate** does not interfere, the procedure is applicable to foods and has been tested on normal and opaque-2 maize meals and on **wheat** flours.

L17 ANSWER 13 OF 13 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1970:411967 HCAPLUS
DOCUMENT NUMBER: 73:11967
TITLE: Release from alveolar macrophages of an inhibitor of phagocytosis
AUTHOR(S): Ulrich, Frank; Zilversmit, Donald B.
CORPORATE SOURCE: Grad. Sch. of Nutr., Cornell Univ., Ithaca, NY, USA
SOURCE: American Journal of Physiology (**1970**), 218(4), 1118-27
CODEN: AJPHAP; ISSN: 0002-9513
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Rabbit alveolar macrophages were incubated in suspension in Krebs-Ringer-phosphate buffer (pH 7.4) at either 0 or 37°. In order to differentiate latex uptake at 0° (binding) from uptake at 37° (ingestion), alveolar macrophages were treated with trypsin and **DNase** following incubation with the particles. The trypsin-**DNase** released 87-93% of the latex taken up at 0° but only 12-21% of the particles taken up at 37°. Trypsin-**DNase** treatment of macrophages after incubation with particles would appear to be a useful method for differentiating between binding and ingestion of particles by these cells. During incubation of the macrophages at either 0° or 37°, a material appeared in the cell supernatant that inhibited the subsequent uptake of cholesterol particles and polystyrene latex particles. This material, which contains both **carbohydrates** and protein, is nondialyzable, soluble in 10% HClO4, and is not destroyed by **heating** for 1 hr at 80°. A fraction with similar activity was isolated also from **human** plasma, rabbit serum, and from rabbit erythrocytes by repeatedly washing the cells with 0.9% NaCl. The inhibition of particle uptake produced by this material was significantly greater at 0° than at 37°. The inhibitor from the lung does not appear to be either an exudate of serum or lung surfactant.

```
=> d que stat l16
L7             1 SEA FILE=REGISTRY ABB=ON  DNASE/CN
L8             1 SEA FILE=REGISTRY ABB=ON  PHOSPHODIESTERASE/CN
L9         45218 SEA FILE=HCAPLUS ABB=ON  L7 OR L8 OR ?DNASE? OR ?PHOSPHODIESTER
                 ASE?
L10          473 SEA FILE=HCAPLUS ABB=ON  L9 AND (?POLYDEOXYRIBONUCLEIC?(W)?ACID
                 ? OR ?MONOSACCH? OR ?CARBOHYDRAT?)
L11          103 SEA FILE=HCAPLUS ABB=ON  L10 AND ?HUMAN?
L12           30 SEA FILE=HCAPLUS ABB=ON  L11 AND (?THERM? OR ?HEAT? OR ?TEMP?)
L13           15 SEA FILE=HCAPLUS ABB=ON  L12 AND (?STABLE? OR ?MINIMIZ? OR
                 ?PRECIP? OR ?CLEAR?)
L14           30 SEA FILE=HCAPLUS ABB=ON  L12 OR L13
L15           68 SEA L14
L16           49 DUP REMOV L15 (19 DUPLICATES REMOVED)

=> d ibib abs l16 1-49

L16  ANSWER 1 OF 49  EMBASE  COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.
     on STN
ACCESSION NUMBER:    2004091597  EMBASE
TITLE:               Transcriptional Regulation of Genes Encoding
                     Arabinan-Degrading Enzymes in Bacillus subtilis.
AUTHOR:              Raposo M.P.; Inacio J.M.; Mota L.J.; De Sa-Nogueira I.
CORPORATE SOURCE:    I. De Sa-Nogueira, Inst. de Tecn. Quimica e Biologica,
                     Universidade Nova de Lisboa, Avenida da Republica, 2781-901
                     Oeiras, Portugal. sanoguei@itqb.unl.pt
SOURCE:              Journal of Bacteriology, (2004) 186/5 (1287-1296).
                     Refs: 42
                     ISSN: 0021-9193  CODEN: JOBAAY
COUNTRY:             United States
DOCUMENT TYPE:       Journal; Article
FILE SEGMENT:        004     Microbiology
LANGUAGE:            English
SUMMARY LANGUAGE:    English
AB   Bacillus subtilis produces hemicellulases capable of releasing arabinosyl
     oligomers and arabinose from plant cell walls. In this work, we
     characterize the transcriptional regulation of three genes encoding
     arabinan-degrading enzymes that are clustered with genes encoding enzymes
     that further catabolize arabinose. The abfA gene comprised in the
     metabolic operon araABDLMNPQ-abfA and the xsa gene located 23 kb
     downstream most probably encode α -L-arabinofuranosidases (EC
     3.2.1.55). Here, we show that the abnA gene, positioned immediately
     upstream from the metabolic operon, encodes an endo-α-1,5-
     arabinanase (EC 3.2.1.99). Furthermore, by in vivo RNA studies,
     we inferred that abnA and xsa are monocistronic and are transcribed from
     σ(A)-like promoters. Transcriptional fusion analysis revealed that
     the expression of the three arabinases is induced by arabinose and
     arabinan and is repressed by glucose. The levels of induction by arabinose
     and arabinan are higher during early postexponential growth, suggesting a
     temporal regulation. Moreover, the induction mechanism of these
     genes is mediated through negative control by the key regulator of
     arabinose metabolism, AraR. Thus, we analyzed AraR-DNA interactions by in
     vitro quantitative DNase I footprinting and in vivo analysis of
     single-base-pair substitutions within the promoter regions of xsa and
     abnA. The results indicate that transcriptional repression of the abfA and
     xsa genes is achieved by a tightly controlled mechanism but that the
     regulation of abnA is more flexible. We suggest that the expression of
     genes encoding extracellular degrading enzymes of arabinose-containing
     polysaccharides, transport systems, and intracellular enzymes involved in
     further catabolism is regulated by a coordinate mechanism triggered by
```

arabinose via AraR.

L16 ANSWER 2 OF 49 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2003134292 EMBASE
TITLE: Purification and properties of hydrophilic dimers of acetylcholinesterase from mouse erythrocytes.
AUTHOR: Gomez J.L.; Nieto-Ceron S.; Campoy F.J.; Munoz-Delgado E.; Vidal C.J.
CORPORATE SOURCE: C.J. Vidal, Depto. de Bioquim. y Biol. Molec.-A, Edificio de Veterinaria, Universidad de Murcia, Apdo. 4021, E-30071 Murcia, Spain. cevidal@um.es
SOURCE: International Journal of Biochemistry and Cell Biology, (1 Jul 2003) 35/7 (1109-1118).
Refs: 41
ISSN: 1357-2725 CODEN: IJBBFU
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Differences in the glycosylation of acetylcholinesterase (AChE) subunits which form the dimers of mouse erythrocyte and a suitable procedure to purify the enzyme by affinity chromatography in edrophonium-Sepharose are described. AChE was extracted (.apprx.80%) from erythrocytes with Triton X-100 and sedimentation analyses showed the existence of amphiphilic AChE dimers in the extract. The AChE dimers were converted into monomers by reducing the disulfide bond which links the enzyme subunits. Lectin interaction studies revealed that most of the dimers were bound by concanavalin A (Con A) (90-95%), Lens culinaris agglutinin (LCA) (90-95%), and **wheat** germ (Triticum vulgaris) agglutinin (WGA) (70-75%), and a small fraction by Ricinus communis agglutinin (RCA(120)) (25-30%). The lower level of binding of the AChE monomers with WGA (55-60%), and especially with RCA (10-15%), with respect to the dimers, reflected heterogeneity in the sugar composition of the glycans linked to each AChE subunit in dimers. Forty per cent of the amphiphilic AChE dimers lost the glycosylphosphatidylinositol (GPI) and, therefore, were converted into hydrophilic forms, by incubation with phosphatidylinositol-specific phospholipase C (PIPLC), which permitted their separation from the amphiphilic variants in octyl-Sepharose. Only the hydrophilic dimers, either isolated or mixed with the amphiphilic forms, were bound by edrophonium-Sepharose, which allowed their purification (4800-fold) with a specific activity of 7700U/mg protein. The identification of a single protein band of 66kDa in gel electrophoresis demonstrates that the procedure can be used for the purification of GPI-anchored AChE, providing that the attached glycolipid domain is susceptible to PIPLC.

L16 ANSWER 3 OF 49 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2003515803 EMBASE
TITLE: Management of bacterial keratitis: Beyond exorcism towards consideration of organism and host factors.
AUTHOR: O'Brien T.P.
CORPORATE SOURCE: T.P. O'Brien, Ocular Infectious Diseases, Wilmer Ophthalmological Institute, Johns Hopkins Univ. Sch. of Medicine, Baltimore, MD, United States. tobrien@jhmi.edu
SOURCE: Eye, (2003) 17/8 (957-974).
Refs: 149
ISSN: 0950-222X CODEN: EYEEEC

COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 004 Microbiology
005 General Pathology and Pathological Anatomy
012 Ophthalmology
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB In summary, the pathogenesis of bacterial keratitis initially requires the adherence of bacteria to disrupted or normal corneal epithelium. Adhesins are microbial proteins that direct the high-affinity binding to specific cell-surface components. These adhesins are able to promote bacterial entry into the host cell, derange leucocyte migration, activate plasmin, and induce cytokine production. In addition, they may act as toxins directly. Adhesins recognize **carbohydrate** and protein moieties on the host cell surface. Most bacteria can display a number of adhesins. Although the cognate oligosaccharides for bacterial adhesins are known, the molecules bearing these determinants are not well characterized. Integrins are a family of glycoproteins mediating cell-cell and cell-extracellular matrix recognition. Many bacterial pathogens have co-opted the existing integrin-based system masking ancillary ligand recognition in a form of mimicry. Once the bacterial pathogen has adhered to the corneal epithelial surface, the next step in establishing infection is invasion into the corneal stroma. Bacterial invasion is facilitated by proteinases that degrade basement membrane and extracellular matrix and cause cell lysis. Proteinases may be derived from bacteria, corneal cells, and migrating leucocytes. Corneal matrix metalloproteinases are excreted in an inactive form, but are activated during infection by bacterial proteinase. Corneal proteinase production may also be induced during the course of infection. The invasion of bacteria into the cornea is facilitated by a number of exotoxins, including P. aeruginosa phospholipase, **heat-stable** haemolysin, and exotoxin-A, which leads to stromal necrosis. Once the bacterial invasion into the cornea has ensued, infection is further facilitated by a complex sequence leading to interruption of the host immune response. Exopolysaccharide formation by both Gram-positive and Gram-negative bacteria results in local immunosuppressive effects. Certain bacteria with capsular polysaccharide also have immunosuppressive properties, including interference with phagocytosis. Proteases degrade complement components, immunoglobulins, and cytokines and may inhibit leucocyte chemotaxis and lymphocyte function. Toxin-A inhibits protein synthesis much as diphtheria toxin by catalysing the transfer of ADPR portion of nicotinamide dinucleotide to mammalian elongation factor-II. Exoenzyme-S is another ADP-ribosyl transferase that may act as an adhesin and also contribute to dissemination of the organism. Two specific bacterial proteases, elastase and alkaline protease, cause marked destruction of the cornea when injected intrastromally. Intrastromal injection of purified elastase alone also results in severe corneal damage. Inhibition of elastase activity with 2-mercaptoacetyl-L-phenylalanine-L-leucine prevents keratolysis. The proteases contribute to the pathogenesis of keratitis by degrading basement membrane, laminin, proteoglycans, extracellular matrix, and collagen. In addition, the bacterial proteases inhibit host defense systems by degrading immunoglobulins, interferon, complement, IL-I, IL-II, and TNF. Such interference results in decreased neutrophil chemotaxis, T-lymphocyte function, and NK cell function. Mutants deficient for alkaline protease do not establish corneal infection, suggesting that this protease is an important initiating factor. A bacterial **heat**-labile phospholipase C has been shown in antibody/substrate specificity studies to be produced in mouse ocular infections suggesting its role as a

potential virulence factor. Bacterial lipopolysaccharide (LPS) stimulates neutrophil migration and infiltration into the cornea with subsequent corneal scarring and opacification. Bacterial exotoxins are released by actively replicating organisms and some endotoxins are released only after the death of the organism. These enzymes and toxins have been shown to persist in the cornea for a protracted period and continue to cause stromal destruction after the death of the pathogen. Most of the bacterial exotoxins are **thermal** labile and have antigenic properties.
Gram-positive bacteria elaborate a variety of biologically active and immunologically distinct toxins. Coagulase-positive strains of Staphylococci are the most pathogenic and elaborate other extracellular enzymes, such as staphylokinase, lipase, hyaluronidase, **DNase**, coagulase, and lysozyme. Coagulase-negative Staphylococci, including S. epidermidis also produce potentially destructive toxin. Streptococcal toxins include Streptolysin O and S, erythrogenic toxin and the enzymes hyaluronidase, streptodornase, and streptokinase. The invasiveness of S. pneumoniae is aided by collagenase activity, although the organism may be inherently invasive without toxin production.

L16 ANSWER 4 OF 49 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2003158791 EMBASE
TITLE: The inhibitory action of pyrrolidine alkaloid, 1,4-dideoxy-1,4-imino-D-ribitol, on eukaryotic DNA polymerases.
AUTHOR: Mizushina Y.; Xu X.; Asano N.; Kasai N.; Kato A.; Takemura M.; Asahara H.; Linn S.; Sugawara F.; Yoshida H.; Sakaguchi K.
CORPORATE SOURCE: Y. Mizushina, Department of Nutritional Science, Lab. of Food/Nutritional Sciences, Kobe-Gakuin University, Nishi-ku, Kobe, Hyogo 651-2180, Japan. mizushin@nutr.kobegakuin.ac.jp
SOURCE: Biochemical and Biophysical Research Communications, (25 Apr 2003) 304/1 (78-85).
Refs: 51
ISSN: 0006-291X CODEN: BBRCA
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The pyrrolidine alkaloids mimicking the structures of pentose with nitrogen in the ring are known to be inhibitors of glycosidases. We report here that a compound belonging to this category is an inhibitor of eukaryotic DNA polymerases. Among the eight naturally occurring pyrrolidine alkaloids we tested, only one compound, 1,4-dideoxy-1,4-imino-D-ribitol (DRB), which was purified from the mulberry tree (Morus alba), strongly inhibited the activities of eukaryotic DNA polymerases with IC(50) values of 21-35μM, and had almost no effect on the activities of prokaryotic DNA polymerases, nor DNA metabolic enzymes such as **human** immunodeficiency virus type 1 reverse transcriptase, T7 RNA polymerase, and bovine deoxyribonuclease I. Kinetic studies showed that inhibition of both DNA polymerases α and β by DRB was competitive with respect to dNTP substrate. Whereas DNA polymerase α inhibition was noncompetitive with the **template**-primer, the inhibition of DNA polymerase β was found to be competitive with the **template**-primer. The K(i) values of DNA polymerases α and β for the **template**-primer were smaller than those for dNTP substrate. Therefore, the affinity of DRB was suggested to be higher at

the **template**-primer binding site than at the dNTP substrate-binding site, although DRB is an analogue of deoxyribose consisting of dNTP. Computational analyses of the eight pyrrolidine alkaloids revealed a remarkable difference in the distribution of positive and negative electrostatic charges on the surface of molecules. The relationship between the structure of DRB and the inhibition of eukaryotic DNA polymerases is discussed. .COPYRGT. 2003 Elsevier Science (USA). All rights reserved.

L16 ANSWER 5 OF 49 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2002056795 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11782910
TITLE: Investigation of protein/**carbohydrate** interactions in the dried state. 1. Calorimetric studies.
AUTHOR: Souillac Pierre O; Costantino Henry R; Middaugh C Russell; Rytting J Howard
CORPORATE SOURCE: The Department of Pharmaceutical Chemistry, The University of Kansas, 2095 Constant Ave., Lawrence, Kansas 66047, USA.
SOURCE: Journal of pharmaceutical sciences, (2002 Jan) 91 (1) 206-16.
Journal code: 2985195R. ISSN: 0022-3549.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200203
ENTRY DATE: Entered STN: 20020125
Last Updated on STN: 20020321
Entered Medline: 20020320

AB Isoperibol calorimetry was used to evaluate protein/**carbohydrate** interactions after freeze drying. rh-**DNase**, rh-GH, rh-MetGH, and rh-IGF-I were freeze dried with either mannitol, sucrose, trehalose, or dextran at concentrations ranging from 0% to 100% (w/w). Enthalpies of solution for both freeze-dried and physical mixtures were measured in water at 25 degrees C. Differential scanning calorimetry was used to monitor changes in the melting or crystallization **temperatures** of the lyoprotectants. Linear relationships between enthalpies of solution and the percentage of protein in the formulations were observed for all physical mixtures. In contrast, nonlinear relationships between the enthalpies of solution and protein content were observed for the freeze-dried mixtures. Mannitol-containing mixtures were characterized by negative deviation from linearity, while positive deviations were detected for mixtures containing sucrose or trehalose. Using DSC, sucrose was found to be amorphous at low and not detected at high protein content in the freeze-dried mixtures. Melting of mannitol was observed through almost all of the protein concentration range examined. Two melting **endotherms**, however, were observed for mannitol at most protein/mannitol ratios, indicating the presence of protein/mannitol interactions. This work suggests that direct interactions occur between proteins and **carbohydrates** in lyophilized mixtures.

L16 ANSWER 6 OF 49 EMBASE on STN
ACCESSION NUMBER: 2001329206 EMBASE
TITLE: Syntheses of anomerically phosphodiester-linked oligomers of the repeating units of the Haemophilus influenzae types c and f capsular polysaccharides.
AUTHOR: Hansson J.; Garegg P.J.; Oscarson S.
CORPORATE SOURCE: S. Oscarson, Department of Organic Chemistry, Arrhenius

Laboratory, Stockholm University, S-106 91 Stockholm, Sweden. s.oscarson@organ.su.se
SOURCE: Journal of Organic Chemistry, (21 Sep 2001) 66/19 (6234-6243).
Refs: 43
ISSN: 0022-3263 CODEN: JOCEAH
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Spacer-equipped dimers and trimers of the repeating units of the capsular polysaccharide of Haemophilus influenzae type c, -4)-3-O-Ac-β-D-GlcpNAc-(1→3)-α-D-Galp-(1-OPO(3) (-)-, and type f, -3)-β-D-GalpNAc-(1→4)-3-O-Ac-α-D-GalpNAc-(1-OPO(3) (-)-, have been synthesized for use in immunological studies. H-Phosphonate chemistry was used for the formation of the interglycosidic phosphate diester linkages. Two types of building blocks, a spacer glycoside disaccharide starting monomer (15 and 22) and an anomeric monoester α-H-phosphonate disaccharide elongating monomer (12 and 27), were built up for each serotype structure from properly protected **monosaccharide** precursors using mainly thioglycosides as glycosyl donors. Stereospecificity in the formation of the α-linked monoester H-phosphonate was possible in type c through crystallization of the pure α-anomer of the precursor hemiacetal from an α/β-mixture, whereas in type f, the hemiacetal was isolated directly as exclusively the α-anomer. Subsequent phosphonylation using triimidazolylphosphine was performed without anomerization. Formation of the anomeric phosphate diester linkages was performed using pivaloyl chloride as coupling reagent followed by I(2)/H(2)O oxidation of the formed diester H-phosphonates. Original experiments afforded no diester product at all, but optimization of the oxidation conditions (lowering the **temperature** and dilution with pyridine prior to I(2) addition) gave the dimers in good yields (71% and 81%) and, subsequently, after removal of a **temporary** silyl protecting group in the dimers, the trimers in fair yields (36% and 37%), accompanied by hydrolysis of the dimer phosphate linkage. One-step deprotection through catalytic hydrogenolysis efficiently afforded the target dimer (30 and 36) and trimer structures (32 and 39). The synthetic scheme allows for further elongation to give higher oligomers.

L16 ANSWER 7 OF 49 EMBASE on STN
ACCESSION NUMBER: 2001188377 EMBASE
TITLE: Phenotypic analysis of genes encoding yeast zinc cluster proteins.
AUTHOR: Akache B.; Wu K.; Turcotte B.
CORPORATE SOURCE: B. Turcotte, Laboratory of Molecular Endocrinol., Royal Victorial Hospital, McGill University, 687 Pine Avenue West, Montreal, Que. H3A 1A1, Canada. turcotte@lan1.molonc.mcgill.ca
SOURCE: Nucleic Acids Research, (15 May 2001) 29/10 (2181-2190).
Refs: 73
ISSN: 0305-1048 CODEN: NARHAD
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Zinc cluster proteins (or **binuclear** cluster proteins) possess

zinc fingers of the Zn(II)2Cys6-type involved in DNA recognition as exemplified by the well-characterized protein GaI4p. These fungal proteins are transcriptional regulators of genes involved in a wide variety of cellular processes including metabolism of compounds such as amino acids and sugars, as well as control of meiosis, multi-drug resistance etc. The yeast (Saccharomyces cerevisiae) sequencing project has allowed the identification of additional zinc cluster proteins for a total of 54. However, the role of many of these putative zinc cluster proteins is unknown. We have performed phenotypic analysis of 33 genes encoding (putative) zinc cluster proteins. Only two members of the GAL4 family are essential genes. Our results show that deletion of eight different zinc cluster genes impairs growth on non-fermentable carbon sources. The same strains are also hypersensitive to the antifungal calcofluor white suggesting a role for these genes in cell wall integrity. In addition, one of these strains (ΔYFL052W) is also **heat** sensitive on rich (but not minimal) plates. Thus, deletion of YFL052W results in sensitivity to a combination of low osmolarity and high **temperature.** In addition, six strains are hypersensitive to caffeine, an inhibitor of the MAP kinase pathway and **phosphodiesterase** of the cAMP pathway. In conclusion, our analysis assigns phenotypes to a number of genes and provides a basis to better understand the role of these transcriptional regulators.

L16 ANSWER 8 OF 49 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN

ACCESSION NUMBER: 2000:363988 BIOSIS
DOCUMENT NUMBER: PREV200000363988
TITLE: In vitro utilization of mucin, lung polymers, plant cell walls and insect cuticle by Aspergillus fumigatus, Metarhizium anisopliae and Haematonectria haematococca.
AUTHOR(S): St. Leger, Raymond J. [Reprint author]; Screen, Steven E.
CORPORATE SOURCE: Department of Entomology, University of Maryland, 4112 Plant Science Building, Baltimore, MD, 20742-4454, USA
SOURCE: Mycological Research, (April, 2000) Vol. 104, No. 4, pp. 463-471. print.
CODEN: MYCRER. ISSN: 0953-7562.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 23 Aug 2000
Last Updated on STN: 8 Jan 2002

AB Aspergillus fumigatus is saprotrophic with an unusual ability to colonize the respiratory tract. The mechanisms that permit pathogenicity may have evolved to adapt the fungus to life as a saprobe. To define the nature of these adaptations and identify common themes in fungal pathogenesis to vertebrates, insects and plants, we compared A. fumigatus with a plant pathogen (Haematonectria haematococca) and an insect pathogen (Metarhizium anisopliae) in their abilities to degrade and utilize host-derived macromolecules (horse lung polymers, porcine mucin, hyaluronic acid, alfalfa cell walls and cockroach cuticle). Each fungus produced a similar range of proteases on mucin and lung polymers, and high levels of several glycosidic enzymes on mucin and plant cell walls, which contain inductive **carbohydrate** substrates. Following 18 h of growth by A. fumigatus at pH 4 or pH 8, the degradation of mucin **carbohydrates** and mucin protein were approximately 40% and 75% respectively, suggesting that the aspartyl proteases (produced at pH 4) and the subtilisin proteases (produced at pH 8) are more important than carbohydrases for degrading mucin. The highly glycosylated mucin residue remaining after 18 h growth resisted further degradation, in part due to bound sialic acid as A. fumigatus secretes a sulphatase but not sialidase. Hyaluronidase activity (an important virulence factor in bacteria) was not produced by A.

fumigatus, M. anisopliae or H. haematococca, but each fungus secreted a range of other enzymes (phospholipase A2, phospholipase C, acid phosphatase, alkali phosphatase, **phosphodiesterase** and esterase) that are common toxic components of bacteria as well as reptilia and invertebrate venoms. Thus **thermotolerant** opportunists such as A. fumigatus may sustain themselves and cause disease in **human** hosts using depolymerases that are widely distributed in fungi and that provide them with the versatility to exploit many environments.

L16 ANSWER 9 OF 49 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2000020088 EMBASE
TITLE: Cyclic AMP mediates the elevation of proline by AKH peptides in the cetoniid beetle, Pachnoda sinuata.
AUTHOR: Auerswald L.; Gade G.
CORPORATE SOURCE: L. Auerswald, Zoology Department, University of Cape Town, Rondebosch 7701, South Africa. lauerswa@botzoo.uct.ac.za
SOURCE: Biochimica et Biophysica Acta - Molecular Cell Research, (2000) 1495/1 (78-89).
Refs: 32
ISSN: 0167-4889 CODEN: BAMRDP
PUBLISHER IDENT.: S 0167-4889(99)00134-2
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 002 Physiology
029 Clinical Biochemistry
003 Endocrinology
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The role of cyclic nucleotides in the transduction of the hyperprolinaemic and hypertrehalosaemic signal of the endogenous neuropeptide Mem-CC was investigated in the cetoniid beetle Pachnoda sinuata. Flight and injection of Mem-CC into the haemocoel of the beetle induce an increase of cAMP levels in the fat body of the beetle. This increase is tissue-specific and does not occur in brain and flight muscles. An elevation of cAMP levels was also found when in vitro preparations of fat body tissue were subjected to Mem-CC. Elevation of the cAMP concentration after injection of Mem-CC is time- and dose-dependent: the maximum response is measured after 1 min, and a dose of 25 pmol Mem-CC is needed. Injection of cpt-cAMP, a cAMP analogue which penetrates the cell membrane, causes a stimulation of proline synthesis but no mobilisation of **carbohydrate** reserves. The same is measured when IBMX, an inhibitor of **phosphodiesterase**, is injected. cGMP seems not to be involved in synthesis of proline nor **carbohydrate** release, because injection of cpt-cGMP has no influence on the levels of proline, alanine and **carbohydrates** in the haemolymph. Although glycogen phosphorylase of the fat body is activated by Mem-CC in a time- and dose-dependent manner, it cannot be stimulated by cpt-cAMP. The combined data suggest that cAMP is involved in regulation of proline levels by Mem-CC but not in regulation of **carbohydrates.** Octopamine has no effect on metabolites in the haemolymph and is not capable of activating glycogen phosphorylase, indicating that it is not involved in the regulation of substrates in this beetle. **Furthermore**, the requirements of the receptor of Mem-CC are different for eliciting a hypertrehalosaemic and a hyperprolinaemic effect, respectively, suggesting that differentiation in signal transduction begins at the receptor level. Copyright (C) 2000 Elsevier Science B.V.

L16 ANSWER 10 OF 49 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 1999410119 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10482393
TITLE: Some properties of alkaline **DNases** of tentacles of actinia Radianthus macrodactylus and their hemolytic activity.
AUTHOR: Gaphurov J M; Bulgakov A A; Galkin V V; Rasskazov V A
CORPORATE SOURCE: Pacific Institute of Bioorganic Chemistry, Far Eastern Division of Russian Academy of Sciences, Vladivostok.
SOURCE: Toxicon : official journal of the International Society on Toxinology, (1999 Nov) 37 (11) 1591-604.
Journal code: 1307333. ISSN: 0041-0101.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199910
ENTRY DATE: Entered STN: 20000111
Last Updated on STN: 20000111
Entered Medline: 19991025

AB Two alkaline **DNases** of tentacles of actinia Radianthus macrodactylus, referred to as alk **DNase** I and alk **DNase** II, respectively, have been purified up to apparent homogeneity with consecutive column ion exchange chromatography and gel filtration. Both enzymes have a lot of common properties, such as the ability to hydrolyze very effectively p-nitrophenyl-5'-TMP and **heat**-denatured DNA. They both have no preferential specificity to the sugar component of the nucleic acids and effectively digest ribopolymers. Their ability to hydrolyze supercoiled DNA of the pBR322 plasmid and linear DNA of the lambda phage by "miscellaneous" exo- and endonucleolytic types of attack and to produce nucleosides, nucleotides and short oligonucleotides suggests their similarity with **phosphodiesterase** I (5'-exonuclease, oligonucleate 5'-nucleotidohydrolase; E.C. 3.1.4.1), isolated from rattle snake Crotalus adamenteus venom. Alk **DNase** II has been revealed to have some uncommon properties, such as phosphomonoesterase and hemolytic activities. The protein causes a very potent lysis of **human** and rabbit erythrocytes. The ability of alk **DNase** II to **precipitate** some components of normal **human** and rabbit blood serum as well as the inhibition of this reaction by fucose but not by another **monosaccharides** suggest the enzyme to have a lectin-like activity. The appearance of only one protein band during electrophoresis of alk **DNase** II in denaturation conditions suggests that all activities are inherent to the same molecule of protein. The possible role of alkaline **DNases** in the toxic effect of burning by actinia tentacles is discussed.

L16 ANSWER 11 OF 49 EMBASE
on STN
ACCESSION NUMBER: 1999288112 EMBASE
TITLE: Mode of action of AraR, the key regulator of L-arabinose metabolism in Bacillus subtilis.
AUTHOR: Mota L.J.; Tavares P.; Sa-Nogueira I.
CORPORATE SOURCE: I. Sa-Nogueira, Inst. Tecnologia Quimica Biologica, Universidade Nova de Lisboa, Apartado 127, 2781-901 Oeiras, Portugal. sanoguei@itqb.unl.pt
SOURCE: Molecular Microbiology, (1999) 33/3 (476-489).
Refs: 34
ISSN: 0950-382X CODEN: MOMIEE
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 004 Microbiology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The AraR protein is a negative regulator involved in L-arabinose-inducible expression of the Bacillus subtilis araABDLMNPQ-abfA metabolic operon and of the araElaraR genes that are organized as a divergent transcriptional unit. The two ara gene clusters are found at different positions in the bacterial chromosome. AraR was overproduced in Escherichia coli and purified to more than 95% homogeneity. AraR binds specifically to DNA fragments carrying the promoter region of the ara genes. **DNase** I protection assays showed that AraR binds to two sequences within the promoters of the araABDLMNPQ-abfA operon and the araE gene, and to one sequence in the araR promoter. The AraR target sequences are palindromic and share high identity, defining a 16 bp AraR consensus operator sequence showing half-symmetry, ATTTGTAC. Binding of AraR to DNA was inhibited by L-arabinose but not by other sugars. The two operator sites within the araABDLMNPQ-abfA operon and araE promoters are located on the same side of the DNA helix, and a pattern of enhanced and diminished **DNase** 1 cleavage was observed between them, but not in the araR promoter. Quantitative **DNase** I footprinting in DNA **templates** containing one, two or three AraR binding sites showed that the repressor binds cooperatively to the two operator sites within the metabolic operon and araE promoters but not to the site located in the araR promoter. These results are consistent with two modes for AraR transcriptional repression that might correlate with different physiological requirements: a high level of repression is achieved by DNA bending requiring two in-phase operator sequences (metabolic operon and araE transport gene), whereas binding to a single operator, which autoregulates araR expression, is 10-fold less effective.

L16 ANSWER 12 OF 49 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 1999:181833 BIOSIS
DOCUMENT NUMBER: PREV199900181833
TITLE: Protein inhalation powders: Spray drying vs spray freeze drying.
AUTHOR(S): Maa, Yuh-Fun [Reprint author]; Nguyen, Phuong-Anh; Sweeney, Theresa; Shire, Steven J.; Hsu, Chung C.
CORPORATE SOURCE: Pharmaceutical Research and Development, Genentech, Inc., 1 DNA Way, South San Francisco, CA, 94080, USA
SOURCE: Pharmaceutical Research (New York), (Feb., 1999) Vol. 16, No. 2, pp. 249-254. print.
CODEN: PHREEB. ISSN: 0724-8741.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 5 May 1999
Last Updated on STN: 5 May 1999

AB Purpose. To develop a new technique, spray freeze drying, for preparing protein aerosol powders. Also, to compare the spray freeze-dried powders with spray-dried powders in terms of physical properties and aerosol performance. Methods. Protein powders were characterized using particle size analysis, **thermogravimetric** analysis, scanning electron microscopy, X-ray powder diffractometry, and specific surface area measurement. Aerosol performance of the powders was evaluated after blending with lactose carriers using a multi-stage liquid impinger or an Anderson cascade impactor. Two recombinant therapeutic proteins currently used for treating respiratory tract-related diseases, deoxyribonuclase (**rhDNase**) and anti-IgE monoclonal antibody (anti-IgE MAb), were employed and formulated with different **carbohydrate** excipients. Results. Through the same atomization but the different drying process,

spray drying (SD) produced small (apprx3 mum), dense particles, but SFD resulted in large (apprx8-10 mum), porous particles. The fine particle fraction (FPF) of the spray freeze-dried powder was significantly better than that of the spray-dried powder, attributed to better aerodynamic properties. Powders collected from different stages of the cascade impactor were characterized, which confirmed the concept of aerodynamic particle size. Protein formulation played a major role in affecting the powder's aerosol performance, especially for the **carbohydrate** excipient of a high crystallization tendency. Conclusions. Spray freeze drying, as opposed to spray drying, produced protein particles with light and porous characteristics, which offered powders with superior aerosol performance due to favorable aerodynamic properties.

L16 ANSWER 13 OF 49 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 97381359 EMBASE
DOCUMENT NUMBER: 1997381359
TITLE: Lipopolysaccharide induces disseminated endothelial apoptosis requiring ceramide generation.
AUTHOR: Haimovitz-Friedman A.; Cordon-Cardo C.; Bayoumy S.; Garzotto M.; McLoughlin M.; Gallily R.; Edwards III C.K.; Schuchman E.H.; Fuks Z.; Kolesnick R.
CORPORATE SOURCE: R. Kolesnick, Laboratory of Signal Transduction, Memorial Sloan-Kettering Can. Center, 1275 York Ave., New York, NY 10021, United States
SOURCE: Journal of Experimental Medicine, (1997) 186/11 (1831-1841).
Refs: 62
ISSN: 0022-1007 CODEN: JEMEAV
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The endotoxic shock syndrome is characterized by systemic inflammation, multiple organ damage, circulatory collapse and death. Systemic release of tumor necrosis factor (TNF)-α and other cytokines purportedly mediates this process. However, the primary tissue target remains unidentified. The present studies provide evidence that endotoxic shock results from disseminated endothelial apoptosis. Injection of lipopolysaccharide (LPS), and its putative effector TNF-α, into C57BL/6 mice induced apoptosis in endothelium of intestine, lung, fat and thymus after 6 h, preceding nonendothelial tissue damage. LPS or TNF-α injection was followed within 1 h by tissue generation of the pro-apoptotic lipid ceramide. TNF-binding protein, which protects against LPS-induced death, blocked LPS-induced ceramide generation and endothelial apoptosis, suggesting systemic TNF is required for both responses. Acid sphingomyelinase knockout mice displayed a normal increase in serum TNF-α in response to LPS, yet were protected against endothelial apoptosis and animal death, defining a role for ceramide in mediating the endotoxic response. **Furthermore**, intravenous injection of basic fibroblast growth factor, which acts as an intravascular survival factor for endothelial cells, blocked LPS-induced ceramide elevation, endothelial apoptosis and animal death, but did not affect LPS-induced elevation of serum TNF-α. These investigations demonstrate that LPS induces a disseminated form of endothelial apoptosis, mediated sequentially by TNF and ceramide generation, and suggest that this cascade is mandatory for evolution of the endotoxic syndrome.

L16 ANSWER 14 OF 49 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN DUPLICATE 3

ACCESSION NUMBER: 1998:4410 BIOSIS
DOCUMENT NUMBER: PREV199800004410
TITLE: Purification and characterization of tilapia (Oreochromis mossambicus) deoxyribonuclease I: Primary structure and cDNA sequence.
AUTHOR(S): Hsiao, Yi-Min; Ho, Heng-Chien; Wang, Wen-Yi; Tam, Ming F.; Liao, Ta-Hsiu [Reprint author]
CORPORATE SOURCE: Inst. Biochem., Coll. Med., Natl. Taiwan Univ., No. 1 Sec. 1 Jen-Ai Rd., Taipei, Taiwan
SOURCE: European Journal of Biochemistry, (Nov., 1997) Vol. 249, No. 3, pp. 786-791. print.
CODEN: EJBCAI. ISSN: 0014-2956.
DOCUMENT TYPE: Article
LANGUAGE: English
OTHER SOURCE: EMBL-AJ001305
ENTRY DATE: Entered STN: 23 Dec 1997
Last Updated on STN: 24 Feb 1998

AB **DNase** I of tilapia (Oreochromis mossambicus) was purified to homogeneity. Tilapia **DNase** I is most active at pH 8.5 with Mg2+ as activator. The Ca2+/Mg2+ pair has a synergistic effect on activation. The enzyme is readily inactivated by **heating** above 55degree C, but is not inactivated by trypsin or 2-mercapto-ethanol under alkaline conditions, with or without CaCl2. Its isoelectric point is 6.0. The 258-amino-acid sequence of tilapia **DNase** I was derived from overlapping sequences of tryptic, chymotryptic and CNBr peptides. The purified enzyme has two variants differing by a single Lys-Arg mutation at position 125. The polypeptide chain has one disulfide bridge and one **carbohydrate** side chain. By mass spectrometry, the purified enzyme shows many molecular mass forms differing by Lys/Arg substitution and sugar-chain length. The major form has a molecular mass of 30914 Da. A 1061-bp nucleotide sequence for the cDNA of tilapia **DNase** I, obtained by gene cloning and DNA sequencing, contains an ORF coding for a putative 26-residue transmembrane peptide and the mature **DNase** I polypeptide.

L16 ANSWER 15 OF 49 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN DUPLICATE 4

ACCESSION NUMBER: 1996:319030 BIOSIS
DOCUMENT NUMBER: PREV199699041386
TITLE: Regulation of fatty acid oxidation by acetyl-CoA generated from glucose utilization in isolated myocytes.
AUTHOR(S): Abdel-Aleem, Salah [Reprint author]; Nada, Mohamed A.; Sayed-Ahmed, Mohamed; Hendrickson, Steven C.; St Louis, James; Walthall, Howard P.; Lowe, James E.
CORPORATE SOURCE: Duke Univ. Med. Cent., Box 3954, Durham, NC 27710, USA
SOURCE: Journal of Molecular and Cellular Cardiology, (1996) Vol. 28, No. 5, pp. 825-833.
CODEN: JMCDAY. ISSN: 0022-2828.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 11 Jul 1996
Last Updated on STN: 11 Jul 1996

AB The regulation of fatty acid oxidation in isolated myocytes was examined by manipulating mitochondrial acetyl-CoA levels produced by **carbohydrate** and fatty acid oxidation. L-carnitine had no effect on the oxidation of (U-14C)glucose, but stimulated oxidation of (1-14C)palmitate in a concentration-dependent manner. L-carnitine (5 mM) increased palmitate oxidation by 37%. The **phosphodiesterase**

inhibitor, enoximone (2 50 mu-M), also increased palmitate oxidation by 51%. Addition of L-carnitine to enoximone resulted in a two-fold increase of palmitate oxidation. Whereas, dichloroacetate (DCA, 1 mM), which stimulates PDH activity, decreased palmitate oxidation by 25%. **Furthermore**, the addition of DCA to myocytes preincubated with either L-carnitine or enoximone, had no effect on the carnitine-induced stimulation of palmitate, and reduced that of enoximone by 50%. Varied concentrations of DCA decreased the oxidation of palmitate and octanoate; but increased glucose oxidation in myocytes. The rate of efflux of acetylcarnitine was highest when pyruvate was present in the medium compared to efflux rates in presence of palmitate or palmitate plus glucose. Although the addition of L-carnitine plus enoximone resulted in a two-fold increase in palmitate oxidation, acetylcarnitine efflux was minimal under these conditions. Acetylcarnitine efflux was highest when pyruvate was present in the medium. These rates were dramatically decreased when myocytes were preincubated with enoximone, despite the stimulation of palmitate oxidation by this compound. These data suggest that: (1) fatty acid oxidation is influenced by acetyl-CoA produced from pyruvate metabolism; (2) L-carnitine may be specific for mitochondrial acetyl-CoA derived from pyruvate oxidation; and (3) it is probable that acetyl-CoA from beta-oxidation of fatty acids is directly channeled into the citric acid cycle.

L16 ANSWER 16 OF 49 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN DUPLICATE 5

ACCESSION NUMBER: 1996:188372 BIOSIS
DOCUMENT NUMBER: PREV199698744501
TITLE: H2-M3-wt-restricted, Listeria-monocytogenes-specific CD8 T cells recognize a novel, hydrophobic, protease-resistant, periodate-sensitive antigen.
AUTHOR(S): Nataraj, Chandrasekaran; Brown, Melinda L.; Poston, Rebecca M.; Shawar, Said M.; Rich, Robert R.; Lindahl, Kirsten Fischer; Kurlander, Roger J. [Reprint author]
CORPORATE SOURCE: Departments Medicine Immunology, Duke University Medical Center, Durham, NC 27710, USA
SOURCE: International Immunology, (1996) Vol. 8, No. 3, pp. 367-378.
ISSN: 0953-8178.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 29 Apr 1996
Last Updated on STN: 29 Apr 1996

AB Mice infected with Listeria monocytogenes (LM) generate H2-M3-wt-restricted CD8 effectors which recognize a **heat**-killed LM-associated antigen (HAA) presented by macrophages. To characterize HAA, we extracted a bioactive component from LM using SDS or NaOH. Extracted HAA aggregated in hydrophilic solvents but dissociated in the presence of SDS into a smaller subunit which migrated in Sephadex G-200 between chymotrypsinogen (25 kDa) and cytochrome c (12.5 kDa). HAA bioactivity and size was unaffected by proteinase K under conditions which degraded virtually all detectable protein. HAA was also unaffected by other proteases, RNase and **DNase**, but HAA bioactivity was destroyed by periodate, an agent that degrades **carbohydrates.** These studies demonstrate that H2-M3-wt can present a hydrophobic, non-peptide, microbial antigen, probably glycolipid in origin, to CD8 T cells.

L16 ANSWER 17 OF 49 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN DUPLICATE 6

ACCESSION NUMBER: 1995:260461 BIOSIS

DOCUMENT NUMBER: PREV199598274761
TITLE: Enhancement of hepatic glucose release and bile flow by the **phosphodiesterase**-III-inhibitor enoximone in the perfused rat liver.
AUTHOR(S): Weidenbach, H. [Reprint author]; Beckh, K.; Schricker, T.; Georgieff, M.; Adler, G.
CORPORATE SOURCE: Dep. Internal Med., Univ. Ulm, Robert Koch Str. 8, D-89081 Ulm, Germany
SOURCE: Life Sciences, (1995) Vol. 56, No. 20, pp. 1721-1726. CODEN: LIFSAK. ISSN: 0024-3205.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 13 Jun 1995
Last Updated on STN: 13 Jun 1995

AB The use of **phosphodiesterase**-III-inhibitors (PDI) as inotropic substances in the treatment of cardiac failure can be associated with hyperglycaemia. This phenomenon could be caused by hepatic events induced by PDI. The purpose of our study was to investigate the effects of the PDI enoximone on hepatic **carbohydrate** metabolism and bile flow. In the rat liver perfusion model, hepatic glucose and lactate production, portal flow and bile flow were determined. Administration of enoximone (1, 10, 100 mu-M) increased hepatic glucose output and bile acid-independent bile flow in a dose-dependent manner. The PDI enhanced the glycogenolytic effects of glucagon (from 15.7 to 38.6 mu-mol glucose/g/20 min), of epinephrine (from 7.1 to 38.7 mu-mol glucose/g/20 min), of norepinephrine (from 9.8 to 32 mu-mol/g/20 min) and of phenylephrine (from 25.5 to 40.8 mu-mol glucose/g/20 min). **Furthermore**, lactate production was significantly reduced by enoximone. The effect of epinephrine and phenylephrine on portal flow was blocked or diminished by enoximone administration. In summary, it was shown that the PDI enoximone is able to enhance hepatic glucose production. Bile acid-independent bile flow was increased by the inhibition of **phosphodiesterase**-III. The effects of enoximone and glycogenolytic hormones on glucose release were synergistic. The vasoconstrictive action of catecholamines was reduced or completely prevented by enoximone. In conclusion, enoximone has glycogenolytic, vasodilatory and choleretic properties in the liver.

L16 ANSWER 18 OF 49 MEDLINE on STN
ACCESSION NUMBER: 94179401 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7510711
TITLE: Expression of a beta 1-related integrin by oligodendroglia in primary culture: evidence for a functional role in myelination.
AUTHOR: Malek-Hedayat S; Rome L H
CORPORATE SOURCE: Department of Biological Chemistry, UCLA School of Medicine 90024-1737.
CONTRACT NUMBER: HD-06576 (NICHD)
HD-07032 (NICHD)
SOURCE: Journal of cell biology, (1994 Mar) 124 (6) 1039-46. Journal code: 0375356. ISSN: 0021-9525.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199404
ENTRY DATE: Entered STN: 19940428
Last Updated on STN: 19960129
Entered Medline: 19940418

AB We have investigated the expression of integrins by rat oligodendroglia

grown in primary culture and the functional role of these proteins in myelinogenesis. Immunochemical analysis, using antibodies to a number of alpha and beta integrin subunits, revealed that oligodendrocytes express only one detectable integrin receptor complex (alpha OL beta OL). This complex is **immunoprecipitated** by a polyclonal anti-**human** beta 1 integrin subunit antibody. In contrast, astrocytes, the other major glial cell type in brain, express multiple integrins including alpha 1 beta 1, alpha 3 beta 1, and alpha 5 beta 1 complexes that are immunologically and electrophoretically indistinguishable from integrins expressed by rat fibroblasts. The beta subunit of the oligodendrocyte integrin (beta OL) and rat fibroblast beta 1 have different electrophoretic mobilities in SDS-PAGE. However, the two beta subunits appear to be highly related based on immunological cross-reactivity and one-dimensional peptide mapping. After removal of N-linked **carbohydrate** chains, beta OL and beta 1 comigrated in SDS-PAGE and peptide maps of the two deglycosylated subunits were identical, suggesting differential glycosylation of beta 1 and beta OL accounts entirely for their size differences. The oligodendrocyte alpha subunit, alpha OL, was not **immunoprecipitated** by antibodies against well characterized alpha chains which are known to associate with beta 1 (alpha 3, alpha 4, and alpha 5). However, an antibody to alpha 8, a more recently identified integrin subunit, did **precipitate** two integrin subunits with electrophoretic mobilities in SDS-PAGE identical to alpha OL and beta OL. Functional studies indicated that disruption of oligodendrocyte adhesion to a glial-derived matrix by an RGD-containing synthetic peptide resulted in a substantial decrease in the level of mRNAs for several myelin components including myelin basic protein (MBP), proteolipid protein (PLP), and cyclic nucleotide **phosphodiesterase** (CNP). These results suggest that integrin-mediated adhesion of oligodendrocytes may trigger signal(s) that induce the expression of myelin genes and thus influence oligodendrocyte differentiation.

L16 ANSWER 19 OF 49 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN

ACCESSION NUMBER: 1993:365476 BIOSIS
DOCUMENT NUMBER: PREV199396051151
TITLE: **Carbohydrate** regulation of the rat L-type pyruvate kinase gene requires two **nuclear** factors: LF-A1 and a member of the c-myc family.
AUTHOR(S): Liu, Zheru; Thompson, Kimberly S.; Towle, Howard C. [Reprint author]
CORPORATE SOURCE: 4-225 Millard Hall, Dep. Biochem., Minneapolis, MN 55455, USA
SOURCE: Journal of Biological Chemistry, (1993) Vol. 268, No. 17, pp. 12787-12795.
CODEN: JBCHA3. ISSN: 0021-9258.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 6 Aug 1993
Last Updated on STN: 8 Aug 1993

AB Transcription of the L-type pyruvate kinase (L-PK) gene is induced in response to increased **carbohydrate** metabolism in the liver. We have demonstrated previously that a segment of the 5'-flanking region of the L-PK gene between -183 and -96 is necessary and sufficient for the glucose response in primary hepatocytes. To explore the protein factors that are involved in **carbohydrate** regulation, we have performed mutational analyses and in vitro binding studies of this segment. Sequences critical for the glucose response were mapped from -171 to -124. This segment contains the consensus binding sites for two **nuclear** transcription factors: LF-A1 and MLTF. Both factors are capable of

binding to the corresponding L-PK sites in vitro. Mutational and functional analyses indicated that LF-A1 is indeed involved in glucose induction of the L-PK gene. The PK MLTF-like site consists of two imperfect CACGTG motifs, the core binding site for a family of transcription factors related to c-myc. Unexpectedly, mutations in either motif that resulted in defective glucose stimulation retained in vitro binding to MLTF. **Furthermore**, an authentic MLTF binding site from the adenovirus major late promoter was not functionally interchangeable with the natural sequence. These data indicate that binding of MLTF, in presence of LF-A1, is not capable of supporting the glucose response. Conversion of either imperfect motif to CACGTG within the context of the mutations disrupting the opposite site restored the response to elevated glucose. Thus, the factor that recognizes the PK MLTF-like site and participates in mediating the **carbohydrate** response of the L-PK gene appears to be a member of the c-myc family distinct from MLTF.

L16 ANSWER 20 OF 49 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 93262794 EMBASE
DOCUMENT NUMBER: 1993262794
TITLE: Strategies to counteract readjustments toward lower metabolic rates during obesity management.
AUTHOR: Dulloo A.G.
CORPORATE SOURCE: Department of Physiology, Faculty of Medicine, University of Geneva, 9 Avenue de Champel/1,1211 Geneva 4, Switzerland
SOURCE: Nutrition, (1993) 9/4 (366-372).
ISSN: 0899-9007 CODEN: NUTRER
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 017 Public Health, Social Medicine and Epidemiology
029 Clinical Biochemistry
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English

L16 ANSWER 21 OF 49 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 93130188 EMBASE
DOCUMENT NUMBER: 1993130188
TITLE: Polyphosphate present in DNA preparations from filamentous fungal species of Colletotrichum inhibits restriction endonucleases and other enzymes.
AUTHOR: Rodriguez R.J.
CORPORATE SOURCE: Department of Plant Pathology, University of California,Riverside, CA 92521, United States
SOURCE: Analytical Biochemistry, (1993) 209/2 (291-297).
ISSN: 0003-2697 CODEN: ANBCA2
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB During the development of a procedure for the isolation of total genomic DNA from filamentous fungi (Rodriguez, R.J., and Yoder, O.C., Exp. Mycol. 15, 232-242, 1991) a cell fraction was isolated which inhibited the digestion of DNA by restriction enzymes. After elimination of DNA, RNA, proteins, and lipids, the active compound was purified by gel filtration to yield a single fraction capable of complete inhibition of restriction enzyme activity. The inhibitor did not absorb uv light above 220 nm, and

was resistant to alkali and acid at 25°C and to **temperatures** as high as 100°C. More extensive analyses demonstrated that the inhibitor was also capable of inhibiting T4 DNA ligase and TaqI DNA polymerase, but not **DNase** or RNase. Chemical analyses indicated that the inhibitor was devoid of **carbohydrates**, proteins, lipids, and nucleic acids but rich in phosphorus. A combination of **nuclear** magnetic resonance, metachromatic shift of toluidine blue, and gel filtration indicated that the inhibitor was a polyphosphate (polyP) containing approximately 60 phosphate molecules. The mechanism of inhibition appeared to involve complexing of polyP to the enzymatic proteins. All species of Colletotrichum analyzed produced polyP equivalent in chain length and concentration. A modification to the original DNA extraction procedure is described which eliminates polyP and reduces the time necessary to obtain DNA of sufficient purity for restriction enzyme digestion and TaqI polymerase amplification.

L16 ANSWER 22 OF 49 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 94089225 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8265200
TITLE: K-antigens in Porphyromonas gingivalis are associated with virulence.
AUTHOR: van Winkelhoff A J; Appelmelk B J; Kippuw N; de Graaff J
CORPORATE SOURCE: Department of Oral Microbiology, Academic Centre for Dentistry Amsterdam (ACTA), The Netherlands.
SOURCE: Oral microbiology and immunology, (1993 Oct) 8 (5) 259-65. Journal code: 8707451. ISSN: 0902-0055.
PUB. COUNTRY: Denmark
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Dental Journals
ENTRY MONTH: 199401
ENTRY DATE: Entered STN: 19940209
Last Updated on STN: 19940209
Entered Medline: 19940127

AB We investigated antigens in spreading and non-spreading Porphyromonas gingivalis strains. On the basis of differences in virulence in the mouse model, 8 strains were selected for antiserum production in rabbits. Hyperimmune sera were tested by double **immunoprecipitation** and immunoelectrophoresis. Besides a common antigen, differences in antigenic composition were observed in the **thermolabile** antigens between all strains tested. Two different **heat-stable** antigens were found after **heating** at 120 degrees C. One such antigen was detected after sonication of the pellet fraction of autoclaved P. gingivalis cells. This antigen cross-reacted with 6 of the 8 immune sera. This somatic antigen was almost neutrally charged and sensitive to sodium periodate treatment, suggestive of lipopolysaccharide. A second **heat-stable** antigen was detected in the supernatant of autoclaved strains of W83, W50, HG184 and A7A1-28. These non-somatic antigens were strain-specific, i.e., no cross-reactivity was found with heterologous hyperimmune sera. An exception was strain W50, which had a non-somatic **heat-stable** antigen which was recognized by W83 antiserum. These antigens were resistant to **DNAse**, RNAse and proteinase-K treatment but were degraded by sodium periodate. In immunoelectrophoresis, these antigens appeared to be negatively charged. These properties are characteristics of a K-antigen, which likely represent a **thermostable carbohydrate** capsule. The presence of K-antigen correlates very well with the serum resistance, the low chemiluminescence, the resistance to phagocytosis and the need for opsonization with specific antibodies for complement-mediated killing of virulent P. gingivalis strains.(ABSTRACT TRUNCATED AT 250 WORDS)

L16 ANSWER 23 OF 49 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN DUPLICATE 8

ACCESSION NUMBER: 1992:389612 BIOSIS
DOCUMENT NUMBER: PREV199294061787; BA94:61787
TITLE: DEFINITION OF THE **CARBOHYDRATE** RESPONSE ELEMENT OF THE RAT S-14 GENE EVIDENCE FOR A COMMON FACTOR REQUIRED FOR **CARBOHYDRATE** REGULATION OF HEPATIC GENES.
AUTHOR(S): SHIH H-M [Reprint author]; TOWLE H C
CORPORATE SOURCE: 4-225 MILLARD HALL, DEP BIOCHEM, UNIV MINN, MINNEAPOLIS, MINN 55455, USA
SOURCE: Journal of Biological Chemistry, (1992) Vol. 267, No. 19, pp. 13222-13228.
CODEN: JBCHA3. ISSN: 0021-9258.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 24 Aug 1992
Last Updated on STN: 25 Aug 1992

AB The 5'-flanking region of the S14 gene from -4316 to +18 contains regulatory sequences responsible for activation of promoter activity in response to elevated **carbohydrate** metabolism in primary hepatocytes. To map these sequences, a series of constructs containing various internal deletions of the S14 5'-flanking sequence were assayed in primary hepatocytes. The region from -1601 to -1395 was found to be essential for this response. Comparison of the sequence of this S14 region to a region of the L-type pyruvate kinase gene that has been shown to mediate **carbohydrate** regulation (Thompson, K. S., and Towle, H. C. (1991) J. Biol. Chemical 266, 8679-8682) revealed a segment with 9 out of 10 identity. In both cases, this conserved sequence aligned with a **DNase** I footprint formed with hepatic **nuclear** extract. Oligonucleotides (.apprx. 30 base pairs) from either S14 or pyruvate kinase genes containing the conserved element bound to a hepatic **nuclear** factor(s) that gave identical complexes by mobility shift assay. **Furthermore**, these two oligonucleotides cross-competed for binding to the **nuclear** factor(s), suggesting that a common factor(s) binds to this conserved element. Reinsertion of the S14 oligonucleotide into an unresponsive S14 promoter construct restored the **carbohydrate** control. Moreover, this oligonucleotide could confer a glucose response when fused to a heterologous promoter. Thus, the S14 segment from -1457 to -1428 is a **carbohydrate** response element essential for the binding of **nuclear** factor(s) regulated by increased **carbohydrate** metabolism. This factor(s) may be common to the **carbohydrate** regulation of the S14 and pyruvate kinase genes.

L16 ANSWER 24 OF 49 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 92364694 EMBASE
DOCUMENT NUMBER: 1992364694
TITLE: **Carbohydrate** cycling in signal transduction: Parafusin, a phosphoglycoprotein and possible Ca2+-dependent transducer molecule in exocytosis in Paramecium.
AUTHOR: Subramanian S.V.; Satir B.H.
CORPORATE SOURCE: Dept. of Anatomy/Structural Biology, Albert Einstein College of Medicine,New York, NY 10461, United States
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1992) 89/23 (11297-11301).
ISSN: 0027-8424 CODEN: PNASA6

COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Parafusin, a cytosolic phosphoglycoprotein of M(r) 63,000, is dephosphorylated and rephosphorylated rapidly in a Ca2+-dependent manner upon stimulation of exocytosis in vivo in wild-type (wt) Paramecium. In contrast, the **temperature**-sensitive exocytosis mutant nd9, grown at the nonpermissive **temperature** (27°C), does not exocytose or dephosphorylate parafusin upon stimulation in the presence of Ca2+; grown at the permissive **temperature** (18°C), nd9 cells show a wt phenotype. Parafusin contains two types of phosphorylation sites: one where glucose 1-phosphate is added by an α-glucose-1-phosphate phosphotransferase and removed by a **phosphodiesterase** and one where phosphate from ATP is added directly to a serine residue by a protein kinase and removed by a phosphatase. We show here that, in cell fractions from wt Paramecium, both reactions can be carried out in vitro by using uridine(5'-[β-[35S]-thio])diphospho(1)-glucose (UDP[β35S]-Glc) and [γ-32P]ATP, respectively. The characteristics of these pathways are different. Specifically, in the presence of Ca2+, the amount of UDP[β35S]-Glc label in parafusin is reduced. In contrast, identical labeling experiments with [γ-32P]ATP show that Ca2+ enhances labeling of parafusin. Mg2+ had no appreciable effect on either labeling. Removal of the UDP[β35S]-Glc label on parafusin in the presence of Ca2+ correlates with the in vivo dephosphorylation seen upon exocytosis. Incubations with UDP[β35S]-Glc were then performed with homogenates and nd9 cell fractions grown at 27°C under the ionic conditions used for wt cells. These labelings were not affected by Ca2+, in contrast to results from wt cells but in accord with those obtained earlier with nd9-27 mutant cells in vivo. Factors responsible for both dephosphorylation and Ca2+ sensitivity were found in the high-speed pellet (P2) in wt cells, suggesting that the putative **phosphodiesterase** is in this fraction and that the defect in the mutant nd9- 27 resides in the Ca2+ activation of the **phosphodiesterase.** We conclude that the in vivo dephosphorylation of parafusin that occurs upon exocytosis is a dephosphoglucosylation due to removal of the α-glucose 1-phosphate and more generally that **carbohydrates** on cytoplasmic glycoproteins may be cyclically added and/or removed in response to extracellular stimuli.

L16 ANSWER 25 OF 49 MEDLINE on STN DUPLICATE 9
ACCESSION NUMBER: 92253840 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1579714
TITLE: Chemical inactivation of the Kveim reagent.
AUTHOR: Lyons D J; Donald S; Mitchell D N; Asherson G L
CORPORATE SOURCE: Division of Immunological Medicine, MRC Clinical Research Centre, Harrow, UK.
SOURCE: Respiration; international review of thoracic diseases, (1992) 59 (1) 22-6.
Journal code: 0137356. ISSN: 0025-7931.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199206
ENTRY DATE: Entered STN: 19920619
Last Updated on STN: 19920619
Entered Medline: 19920609

AB In an **attempt** to identify the nature of the active principle, Kveim reagent was exposed to chemical fractionating agents. Thirty-one patients with sarcoidosis underwent simultaneous intradermal injection with fractionated and unfractionated Kveim material. Kveim reagent was **stable** in the presence of **DNAse**, RNAse, pronase, 95% phenol, neutral detergent, and to lipid extraction with chloroform-methanol. Kveim reagent was also **stable** in the presence of both 8 M urea (8MU) and 2-mercaptoethanol (2ME) when used alone. When both these agents were used together, Kveim reagent was inactivated. Fourteen patients had a positive test to unfractionated Kveim reagent; of these, only 2 gave a positive response to material fractionated by exposure to 8MU and 2ME. Simultaneous exposure to 8MU and 2ME was more likely to inactivate Kveim reagent (10/10 tests) than sequential exposure to 8MU and 2ME (2/4 tests). Chemical analysis of the fractionated material showed that it retained granuloma-generating activity despite the lack of **carbohydrates.** Protein loss in terms of total and relative amino acid composition was progressive and non-specific throughout processing. These results are consistent with a protein-active principle which is dependent on three-dimensional structure.

L16 ANSWER 26 OF 49 JICST-EPlus COPYRIGHT 2004 JST on STN
ACCESSION NUMBER: 910634185 JICST-EPlus
TITLE: The Production of Monoclonal Anti-**Human** Spetrin Antibody Cross-Reactive with Single-Stranded DNA.
AUTHOR: MUKAI MASAYA
CORPORATE SOURCE: Hokkaido Univ., School of Medicine
SOURCE: Hokkaido Igaku Zasshi (Hokkaido Journal of Medical Science), (1991) vol. 66, no. 4, pp. 425-440. Journal Code: Z0749A (Fig. 17, Ref. 38)
ISSN: 0367-6102
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article
LANGUAGE: Japanese
STATUS: New

AB Five monoclonal anti-**human** red blood cell(RBC) antibodies (all IgM K type) were prosuced by immunizing BALB/c mouse with **human** O-type RBC. Solid phase enzyme linked immunosorbent assays(ELISAs) were used for studying the reactivities of monoclonal antibodies against RBC, DNA, cardiolopin, dermatan sulfate and spectrin. Because two monoclonal antibodies (1B1A2E5, 1B1B2G7) of these antibodies also reacted with **heat**-denatured DNA (ssDNA) derived from calf thymus, salmon sperm and **human** white blood cell, the crossreactivities of two monoclonal antibodies were analyzed. They reacted with spectrin, one of the RBC cytoskeleton proteins, by western blotting using RBC ghost protein and ELISA using spectrin, but not react with other anionic antigens such as cardiolipin and dermatan sulfate. The anti-RBC activities of the two monoclonal antibodies were not changed by **DNase** I treatment, but were decreased by pronase E treatment of RBC ghost protein. And, the anti-ssDNA activities of these antibodies were abolished by **DNase** I treatment, but were not changed by pronase E treatment of DNA. The reactivities of these antibodies to RBC and ssDNA were inhibited by ssDNA, RBC ghost protein and rabbit anti-mouse IgM antiserum, but were not inhibited by dsDNA, RBC, rabbit anti-mouse IgG antiserum, bovine serum albumin and spectrin in liquid phase. In inhibition test, spectrin in liquid phase did not inhibit the reaction for RBC or ssDNA of these antibodies. Complements were fixed to these antibodies in RBC, ssDNA and spectrin ELISA. In the view of the above results, it was concluded that the RBC antigen of the 2 monoclonal antibodies was directed against spectrin in solid phase, and that these

antibodies were cross-reactive with both RBC (spectrin) and ssDNA (derived from calf thymus, salmon sperm and **human** white blood cell). (author abst.)

L16 ANSWER 27 OF 49 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN DUPLICATE 10

ACCESSION NUMBER: 1991:133715 BIOSIS
DOCUMENT NUMBER: PREV199191070255; BA91:70255
TITLE: CELLULAR METABOLISM OF 3' AZIDO-2' 3'-DIDEOXYURIDINE WITH FORMATION OF 5'-O DIPHOSPHOHEXOSE DERIVATIVES BY PREVIOUSLY UNRECOGNIZED METABOLIC PATHWAYS FOR 2' DEOXYURIDINE ANALOGS.
AUTHOR(S): ZHU Z [Reprint author]; SCHINAZI R F; CHU C K; WILLIAMS G J; COLBY C B; SOMMADOSSI J-P
CORPORATE SOURCE: UAB, DEP PHARMACOL, UNIV STATION, BOX 600, BIRMINGHAM, ALA 35294, USA
SOURCE: Molecular Pharmacology, (1990) Vol. 38, No. 6, pp. 929-938. CODEN: MOPMA3. ISSN: 0026-895X.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 14 Mar 1991
Last Updated on STN: 22 May 1991

AB 3'-Azido-2',3'-dideoxyuridine (AzdU, CS-87) is a potent inhibitor of **human** immunodeficiency virus replication in **human** peripheral blood **mononuclear** cells (PBMC) with limited toxicity for **human** bone marrow cells (BMC). In the present study, metabolism of AzdU was investigated in **human** PBMC and BMC after exposure of cells to 2 or 10 μM [3H]AzdU. 3'-Azido-2',3'-dideoxyuridine-5'-monophosphate (AxdU-MP) was the predominant metabolite, representing approximately 55 to 65% of intracellular radioactiity in both PBMC and BMC at all times. The AzdU-5'-diphosphate and -5'-triphosphate intrcellular levels were 10- to 100-fold lower than the AzdU-MP levels and, of note, AzdU-5'-triphosphate was not detected in **human** BMC. Using anion exchange chromatography, a new peak of radioactivity, distinct from any known anabolites, was detected. This chromatorgraphic peak was found to be resistant to alkaline phosphatase but was hydrolyzed by 5'-**phosphodiesterase**, yielding AzdU-MP. Incubation of [3H]AzdU and D[1-14C]glucose in PBMC and BMC produced a double-labeled peak with the same retention time as the anabolite, suggesting formation of a hexose derivative of AzdU. A novel high performance liquid chromatography method was developed that allowed for the separation of nucleosides, nucleotides, and **carbohydrate** derivates thereof. Using this highly specific method, the putative AzdU-hexose actually was separated into two chromatographic peaks. These novel metabolites were identified as 3'-azido-2',3'-dideoxyuridine-5'-O-diphosphoglucose and 3'-azido-2,'3'-dideoxyuridine-5'-O-diphospho-N-acetylgucosamine. Following 48 hr of incubation with [3H] AzdU, as much as 20 and 30% of these AzdU metabolites accumulated in PBMC and BMC, respectively. When AzdU was removed from the cell cultures, intracellular AzdU diphosphohexose concentrations decayed in a monophasic manner, with an elimination half-life of 14.3 hr. By 48 hr, levels of 0.3 pmol/106 cells were still detected, reflecting a gradual anabolism of these metabolites. Elimination of AzdU-MP and AzdU-5'-diphosphate was characterized by a two-phase process, with a short initial half-life of 0.83 and 0.24 hr and a long terminal half-life of 14.10 and 8.24 hr, respectively. Similar diphosphohexoses of deoxyrudine (dUrd) were also detected in **human** PBMC and BMC after exposure to [3H]dUrd, suggesting that dUrd derivatives are metabolized in a similar manner. In summary, the discovery of novel metabolic pathways for dUrd analogs demonstrates that AzdU has unique

metabolic features that may contribute to the low toxicity of this anti-HIV agent in **human** BMC and also affect its mechanism of action. **Furthermore**, these findings may provide insight into the development of novel **human** immunodeficiency virus antiviral agents.

L16 ANSWER 28 OF 49 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN DUPLICATE 11

ACCESSION NUMBER: 1989:384457 BIOSIS
DOCUMENT NUMBER: PREV198988065047; BA88:65047
TITLE: PURIFICATION AND CHARACTERIZATION OF A BENZODIAZEPINE-LIKE SUBSTANCE FROM MAMMALIAN BRAIN.
AUTHOR(S): LIAO C C [Reprint author]; LIN H S; LIU J-Y; HIBBARD L S; WU J-Y
CORPORATE SOURCE: DEP PHYSIOL, THE MILTON S HERSHEY MED CENT
SOURCE: Neurochemical Research, (1989) Vol. 14, No. 4, pp. 345-352. CODEN: NEREDZ. ISSN: 0364-3190.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 17 Aug 1989
Last Updated on STN: 26 Aug 1989

AB An endogenous brain ligand which competes with [3H]-flunitrazepam for the binding to benzodiazepine receptor has been isolated and purified to homogeneity. The purification procedures involve the extraction of the endogenous ligand by homogenizing the brain tissue in water containing various protease inhibitors followed by filtration through a PM 10 membrane (exclusion limit: 10,000-dalton), column chromatographies on Sephadex G-50, Bio-Rad P2 and a series of C18 reverse phase HPLC columns. The purified endogenous ligand was eluted as a single and symmetrical peak monitored at either 220 or 280 nm. **Furthermore**, the ligand activity coincided with the absorption peak. The purified endogenous ligand is **thermostable**, insensitive to various peptidases and proteolytic enzymes, resistant to **DNAse**, RNAse, and **carbohydrate** enzyme e.g. neuraminidase (EC 3.21.18) and acid treatment. It has a major absorption peak at 220 nm and a minor one at 313 nm. The endogenous ligand appears to be quite specific since it only inhibits the binding of ligand to the central type benzodiazepine receptor but not to other receptors, e.g. peripheral type benzodiazepine receptor, α1-adrenoceptor, α2-adrenoceptor, β-adrenoceptor and muscarinic cholinergic receptor. **Furthermore**, the inhibition of the receptor binding by the endogenous ligand is enhanced by GABA suggesting that the endogenous ligand is a benzodiazepine receptor agonist. The structure of the endogenous ligand is unknown.

L16 ANSWER 29 OF 49 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN

ACCESSION NUMBER: 1988:96445 BIOSIS
DOCUMENT NUMBER: PREV198885053217; BA85:53217
TITLE: PURIFICATION AND CHARACTERIZATION OF **PHOSPHODIESTERASE** EXONUCLEASE FROM CERASTES-CERASTES EGYPTIAN SAND VIPER VENOM.
AUTHOR(S): HALIM H Y [Reprint author]; SHABAN E A; HAGAG M M; DAOUD E W; EL-ASMAR M F
CORPORATE SOURCE: RES UNIT NAT TOXINS, DEP BIOCHEM, FAC MED, AIN SHAMS UNIV, CAIRO, EGYPT
SOURCE: Toxicon, (1987) Vol. 25, No. 11, pp. 1199-1208. CODEN: TOXIA6. ISSN: 0041-0101.
DOCUMENT TYPE: Article
FILE SEGMENT: BA

LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 11 Feb 1988
Last Updated on STN: 11 Feb 1988

AB A venom exonuclease '**phosphodiesterase**' (E.C.3.1.4.1) has been purified from Cerastes cerastes venom by a combination of gel filtration on Sephadex G-100 superfine and ion exchange chromatography on DEAE-Sepharose. The enzyme showed a single band on PAGE and SDS-PAGE and had a molecular weight of 110,000. The final preparation was purified 28 fold. It had no **carbohydrate** and it did not have protease or 5'-nucleotidase activities. Optimum **temperature** for **temperature** for enzyme activity was 56°C. The enzyme was rapidly inactivated when pre-incubated above 40°C. Energy of activation (Eα) was calculated to be 0.913. The optimum pH was 9.0. Cysteine, glutathione, dithiothreitol, 2-mercaptoethanol, ADP and AMP inhibited the enzyme. Cysteine caused a non-competitive inhibition, while ADP showed a competitive inhibition. EDTA at a concentration of 0.5 mM caused complete inhibition of the enzyme, which could be reversed by the addition of Ca2+ or Mn2+.

L16 ANSWER 30 OF 49 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 1986:92582 BIOSIS
DOCUMENT NUMBER: PREV198681002998; BA81:2998
TITLE: THE SUBUNIT STRUCTURE AND ACTIVE SITE SEQUENCE OF PORCINE SPLEEN **DNASE.**
AUTHOR(S): LIAO T-H [Reprint author]
CORPORATE SOURCE: DEPARTMENT OF BIOCHEMISTRY, COLLEGE OF MEDICINE, NATIONAL TAIWAN UNIVERSITY, TAIPEI, TAIWAN
SOURCE: Journal of Biological Chemistry, (1985) Vol. 260, No. 19, pp. 10708-10713.
CODEN: JBCHA3. ISSN: 0021-9258.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 25 Apr 1986
Last Updated on STN: 25 Apr 1986

AB An acid **DNase** (**DNase** II) from porcine spleen was purified by sequential chromatography over carboxy-methyl-cellulose, blue dextran-Sepharose, hydroxylapatite, and sulfoxyethyl-cellulose. The purified enzyme shows two polypeptide bands on sodium dodecyl sulfate-polyacrylamide gel electrophoresis at Mr 35,000 (α chain) and 10,000 (β chain). The sum of the two molecular weights is that of the native enzyme (45,000). Thus, the **DNase** II molecule is an α,β dimer. The two polypeptides are not joined by disulfide bonds, but can be cross-linked chemically with dimethyl suberimidate. They are dissociable in 8 M urea, after which they can be isolated by gel filtration on Sephadex G-100, eluting with 1 M acetic acid. Once dissociated, the two polypeptides cannot be reassociated to regenerate **DNase** II activity. The sum of the amino acid compositions of the two polypeptides is that of the native enzyme, and both contain **carbohydrate.** The β chain is devoid of histidine, half-cystine, valine, and methionine. The NH2-terminal amino acid of the α chain is leucine, while that of the β chain cannot be identified by either dansylation or Edman degradation. Alkylation of an essential histidine residue of **DNase** II occurs on incubation of the enzyme with [2-14C]ICH2COOH (Oshima, R.G., and Price, P.A. (1973) J. Biol. Chemical 248, 7522-7526). Radioactivity is found only in the α chain. After hydrolysis of the α chain with trypsin, chymotrypsin, and **thermolysin**, radioactive peptides were isolated by gel filtration on Sephadex G-25 and reversed-phase high performance liquid

chromatography. Sequence analyses of the radioactive peptides show alkylation of 1 of 9 histidines in the entire amino acid sequence of **DNase** II. The sequence around this histidine, determined by manual microsequencing and by the release of amino acids with carboxypeptidases A and B, is Ala-Thr-Glu-Asp-His-Ser-Lys-Trp.

L16 ANSWER 31 OF 49 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 85130013 EMBASE
DOCUMENT NUMBER: 1985130013
TITLE: Circulating mediators in **thermal** injuries: Isolation and characterization of a burn injury-induced immunosuppressive serum component.
AUTHOR: Ozkan A.N.; Ninnemann J.L.
CORPORATE SOURCE: University of California San Diego School of Medicine, La Jolla, CA, United States
SOURCE: Journal of Burn Care and Rehabilitation, (1985) 6/2 (147-151).
CODEN: JBCRD2
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 034 Plastic Surgery
009 Surgery
004 Microbiology
026 Immunology, Serology and Transplantation
LANGUAGE: English

AB Immunosuppression in **thermally** injured patients is a well-documented phenomenon that significantly contributes to the high incidence of septic episodes. This report reviews the isolation and partial characterization of a burn injury-induced suppressor active peptide (SAP) that is believed to play a critical role in immunosuppression following **thermal** trauma. This SAP complex appears to be a prostanoid carrier complex with the following characteristics: a low molecular weight (between 1,000 and 5,000); a complex composition containing a protein component rich in glycine and serine, a **carbohydrate** moiety containing sialic acid, and a lipid component (which apparently includes arachidonic acid metabolites); a structure that is **heat stable** (56 C for 30 minutes), pH **stable**, and unaffected by treatment with trypsin, proteinase K, **DNAse**, and RNAse; a suppressive mode of action that is dependent on the presence of the lipid moiety (most likely PGE2 since treatment with anti-PGE2 often blocks activity and activity can be restored to the delipidated molecule by reintroduction of PGE2); a noncytotoxic immunosuppressive mode of action; and erythrocyte hemolytic capability that is dependent upon the sialo-peptide component (delipidation does not affect hemolytic activity).

L16 ANSWER 32 OF 49 MEDLINE on STN DUPLICATE 12

ACCESSION NUMBER: 86084350 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3000939
TITLE: Abnormalities of platelet function in hypertension and diabetes.
AUTHOR: Hamet P; Skuherska R; Pang S C; Tremblay J
CONTRACT NUMBER: AM21299 (NIADDK)
SOURCE: Hypertension, (1985 Nov-Dec) 7 (6 Pt 2) II135-42. Ref: 46
Journal code: 7906255. ISSN: 0194-911X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English

FILE SEGMENT: Priority Journals
ENTRY MONTH: 198601
ENTRY DATE: Entered STN: 19900321
Last Updated on STN: 19980206
Entered Medline: 19860130

AB The increased frequency of hypertension in diabetes and of abnormalities of **carbohydrate** metabolism in hypertension are now well established. It is conceivable that the high coincidence of the two diseases is based on a common metabolic defect. Studies of platelets permit the evaluation of the stimulatory, phosphoinositol-linked and the inhibitory, cyclic adenosine 3',5'-monophosphate-dependent pathways of cell activation. **Furthermore**, platelets may be relevant for the development of angiopathy through their contents of growth factors. Abnormalities of platelet aggregation have been demonstrated in hypertension and diabetes. They are accompanied by exaggerated stimulation of adenylate cyclase in hypertension and abnormal activity of cyclic guanosine 3',5'-monophosphate **phosphodiesterase** in diabetes. Defective function of platelets is also observed in patients and animals when the two diseases are present at the same time. Both increased and decreased aggregation have been described in these two diseases in the literature. The apparent discrepancies may be due to different types of platelet preparation, evaluation of aggregation, evolution of defect with age, and form of the disease. Integrated studies of biochemical mechanisms responsible for cell activation are needed to characterize the exact defect present in diabetes and hypertension in platelets.

L16 ANSWER 33 OF 49 MEDLINE on STN DUPLICATE 13
ACCESSION NUMBER: 85134944 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3973938
TITLE: Definition of a burn injury-induced immunosuppressive serum component.
COMMENT: Comment in: NIH Guide Grants Contracts. 1994 Dec 23;23(45):2-3. PubMed ID: 7826680
Erratum in: J Trauma 1994 Oct;37(4):687
AUTHOR: Ninnemann J L; Ozkan A N
CONTRACT NUMBER: GM 29226 (NIGMS)
SOURCE: Journal of trauma, (1985 Feb) 25 (2) 113-7.
Journal code: 0376373. ISSN: 0022-5282.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 198503
ENTRY DATE: Entered STN: 19900320
Last Updated on STN: 19950307
Entered Medline: 19850322

AB We and others have previously observed that immunologic activity can often be restored to both lymphocytes and neutrophils by removing them from the burn environment, leading to the conclusion that burn serum contains substances capable of suppressing immunologic function. The present studies were initiated to better define the serum component(s) responsible for this immunosuppression. The majority of immunosuppressive activity vs. both neutrophil chemotaxis and mixed lymphocyte cultures contained in large-volume serum samples obtained from three patients with greater than 40% body surface area flame burns was found to reside in a less than 25,000 mw fraction of serum obtained by Amicon ultrafiltration. A single suppressive serum component was isolated by **precipitation** and resuspension, followed by ion-exchange chromatography using an SP Sephadex C-25 column. Purity of the samples was verified by SDS slab-gel

electrophoresis, and immunosuppressive activity was confirmed vs. both lymphocytes and neutrophils. Analysis of this isolated burn-associated suppressor indicates: a) a molecular weight of between 1,000 and 5,000 daltons; b) a complex composition containing a protein component, a lipid component, and a **carbohydrate** component; c) a structure which is **heat stable**, pH **stable** and unaffected by treatment with trypsin, proteinase K, **DNAse**, and RNAse; and d) a noncytotoxic immunosuppressive mode of action. It appears that the suppressive activity is dependent upon a prostaglandin portion of this low molecular weight complex.

L16 ANSWER 34 OF 49 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN DUPLICATE 14

ACCESSION NUMBER: 1984:333658 BIOSIS
DOCUMENT NUMBER: PREV198478070138; BA78:70138
TITLE: ACTIVATION OF INSULIN SENSITIVE PHOSPHO DI ESTERASE BY LECTINS AND INSULIN DEXTRAN COMPLEX IN RAT FAT CELLS.
AUTHOR(S): SUZUKI T [Reprint author]; MAKINO H; KANATSUKA A; OSEGAWA M; YOSHIDA S; SAKAMOTO Y
CORPORATE SOURCE: SECOND DEP INTERNAL MED, CHIBA UNIV SCH MED, 1-8-1 INOHANA, CHIBA 280, JPN
SOURCE: Metabolism Clinical and Experimental, (1984) Vol. 33, No. 6, pp. 572-576.
CODEN: METAAJ. ISSN: 0026-0495.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH

AB Membrane-bound low-Km cAMP **phosphodiesterase** was activated by concanavalin A [con A], **wheat** germ agglutinin, and insulin-dextran complex under conditions of incubation with intact rat fat cells. Con A rapidly stimulated the enzyme activities and maximum was reached at 10-15 min. As little as 10 μg/ml con A activated the enzyme and a maximal response was obtained at 100-300 μg/ml, but con A and **wheat** germ agglutinin were less potent than insulin. Specific saccharide inhibitors completely abolished activation of the enzyme by lectins, but had no effect on the activation of insulin. Digestion of fat cells with 1 mg/ml trypsin for 15 min completely inhibited activation of the enzyme by insulin. Con A was less sensitive to trypsinization. The insulin-dextran complex, which did not penetrate the plasma membrane, activated the enzyme and was 1/10 as effective as the native insulin. The insulin-like actions of these lectins are provoked through coupling with the **carbohydrate** moiety on the cell membrane close to insulin receptors.

L16 ANSWER 35 OF 49 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN

ACCESSION NUMBER: 1984:359302 BIOSIS
DOCUMENT NUMBER: PREV198478095782; BA78:95782
TITLE: LECTIN COATED AGAROSE BEADS IN THE INVESTIGATION OF SPERM CAPACITATION IN THE HAMSTER.
AUTHOR(S): AHUJA K K [Reprint author]
CORPORATE SOURCE: MRC EXP EMBRYOL TERATOL UNIT, WOODMANSTERNE ROAD, CARSHALTON, SURREY SM5 4EF, ENGLAND, UK
SOURCE: Developmental Biology, (1984) Vol. 104, No. 1, pp. 131-142.
CODEN: DEBIAO. ISSN: 0012-1606.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH

AB Sperm surface changes during in vitro capacitation were examined with the help of an assay system using lectin-coated agarose beads. The nature and

intensity of binding of epididymal spermatozoa to beads depended entirely on the particular stage of capacitation and the type of lectin attached to the bead surface. Fresh epididymal spermatozoa bound readily to beads coated with Con A, LCA, WGA and PNA [concanavalin A, Lens culinaris agglutinin, **wheat** germ agglutinin and peanut agglutinin, respectively] but not with 7 other lectins. During capacitation there was a constant decline in sperm binding to beads, and spermatozoa cultured for 4-5 h bound only to those coated with Con A. A dramatic increase in sperm binding to Con A-coated agarose beads occurred between 4.5 and 5 h when large numbers of hyperactivated spermatozoa adhered, predominantly through their flagellae, to form large clumps on the beads. The clumping of spermatozoa on Con A-coated beads was enhanced in the presence of stimulators of capacitation (i.e., taurine, hypotaurine and **phosphodiesterase** inhibitors) and was suppressed in the presence of various metabolic inhibitors (i.e., sodium azide and local anesthetics). The implications of these results are that the **carbohydrate** components of the entire surface of spermatozoa undergo striking changes during capacitation, and a close relationship may exist between the sperm surface and the metabolic changes occurring within capacitating spermatozoa. Sperm-bead binding assays are **clearly** able to recognize surface changes in asynchronous populations of motile spermatozoa and, due to their simplicity and speed, should prove to be valuable in gaining a greater understanding of the biochemistry of sperm capacitation.

L16 ANSWER 36 OF 49 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN DUPLICATE 15

ACCESSION NUMBER: 1983:301559 BIOSIS
DOCUMENT NUMBER: PREV198376059051; BA76:59051
TITLE: ACTIN STIMULATED MYOSIN MAGNESIUM II ATPASE INHIBITION BY BRAIN PROTEIN.
AUTHOR(S): BERL S [Reprint author]; CHOU M; MYTILINEOU C
CORPORATE SOURCE: MOUNT SINAI SCH MED, FIFTH AVE AND 100TH ST, NEW YORK, NY 10029, USA
SOURCE: Journal of Neurochemistry, (1983) Vol. 40, No. 5, pp. 1397-1405.
CODEN: JONRA9. ISSN: 0022-3042.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH

AB A low MW protein, isolated from bovine brain, inhibits the actin-stimulated Mg-ATPase activity of myosin from striated muscle. This inhibition is probably related to its ability to cause actin to revert from its polymerized to its depolymerized state and to prevent the polymerization of actin. Its effect on the polymeric state of the actin has been demonstrated by viscosity studies, **DNase** inhibition assay and EM. Heavy meromyosin can overcome the effect of the brain protein and stimulate the polymerization of actin. The inhibition of ATPase activity is in part dependent on the relative amounts of brain protein, actin and myosin. The apparent MW of the brain protein is .apprx. 20,000 daltons. It appears to be a **heat**-labile glycoprotein containing 5-6% **carbohydrate.**

L16 ANSWER 37 OF 49 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 83254089 EMBASE
DOCUMENT NUMBER: 1983254089
TITLE: Purification and characterization of a bacteriocin from Bacteroides fragilis.
AUTHOR: Hayes T.J.; Cundy K.R.; Fernandes P.B.; Hoober K.

CORPORATE SOURCE: Dep. Microbiol. Immunol., Temple Univ. Sch. Med., Philadelphia, PA 19140, United States
SOURCE: Journal of Bacteriology, (1983) 155/3 (1171-1177). CODEN: JOBAAY
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 004 Microbiology
LANGUAGE: English

AB A bacteriocin produced by Bacteroides fragilis 1356 was purified from culture medium and characterized. The spectrum of the inhibitory activity of this bacteriocin was species specific. The bacteriocin was recovered from the initial stages of purification as a complex, greater than 2 x 107 daltons in mass, containing protein, lipid, and **carbohydrate.** The dissociation of this complex by 6.0 M guanidine hydrochloride permitted further purification of the bacteriocin by removal of lipid and **carbohydrate.** Analysis by sodium dodecyl sulfate-polyacrylamide gel electrophoresis indicated that the purified bacteriocin was homogeneous, with a relative molecular weight of 5,000. The activity of the purified bacteriocin was not affected by RNase, **DNase,** phospholipase A, pancreatic lipase, or dextranase, but was destroyed by trypsin, proteinase K, **heat** (80°C, 30 min), or a pH below 5 or above 8. Amino acid analysis indicated a predominance of acidic and polar amino acids.

L16 ANSWER 38 OF 49 MEDLINE on STN DUPLICATE 16
ACCESSION NUMBER: 83236908 MEDLINE
DOCUMENT NUMBER: PubMed ID: 6862628
TITLE: Characterization of Toxoplasma gondii antigens that react with **human** immunoglobulin M and immunoglobulin G antibodies.
AUTHOR: Naot Y; Guptill D R; Mullenax J; Remington J S
CONTRACT NUMBER: AI 04717 (NIAID)
SOURCE: Infection and immunity, (1983 Jul) 41 (1) 331-8. Journal code: 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198308
ENTRY DATE: Entered STN: 19900319
Last Updated on STN: 19970203
Entered Medline: 19830811

AB Studies were performed to define the nature of the Toxoplasma gondii antigens that are recognized by **human** immunoglobulin M (IgM) and IgG antibodies. Both IgM and IgG antibodies were found to be directed mainly against T. gondii membrane antigens in sera obtained from patients with acute toxoplasmosis. Treatment of the membrane preparation with **DNase,** RNase, or lipase had no apparent effect on the reactivity of the membrane antigens with IgM and IgG antibodies. Lipids isolated from tachyzoites were not recognized by either IgM or IgG antibodies. Exposure of T. gondii membranes to **heat,** proteolysis, or oxidation with sodium periodate decreased the reactivity of the membrane preparations with both IgM and IgG antibodies. A preparation of T. gondii proteins and polysaccharides were recognized by both immunoglobulin classes. T. gondii polysaccharides reacted with **human** IgG antibodies produced during both the acute and chronic phases of the infection. We concluded that, after infection with T. gondii, IgM and IgG antibodies are elicited in response to both protein and **carbohydrate** constituents of the invading parasite.

L16 ANSWER 39 OF 49 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 1982:197874 BIOSIS
DOCUMENT NUMBER: PREV198273057858; BA73:57858
TITLE: EFFECTS OF FEEDING ON AMINOPHYLLINE INDUCED SUPRAMAXIMAL **THERMOGENESIS.**
AUTHOR(S): WANG L C H [Reprint author]
CORPORATE SOURCE: DEP ZOOL, UNIV ALBERTA, EDMONTON, ALBERTA T6G 2E9
SOURCE: Life Sciences, (1981) Vol. 29, No. 24, pp. 2459-2466.
CODEN: LIFSAK. ISSN: 0024-3205.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
AB Single injection of aminophylline (a **phosphodiesterase** inhibitor which prolongs cAMP actions) elicited supramaximal **thermogenesis** in cold exposed rats. The increases were 19.4, 16 and 15%, respectively, above their saline-injected self-control maxima in the overnight fasted, rationed, and ad libitum fed states. In the fasted state the increased **thermogenesis** could not be sustained. Feeding of a 5 ml substrate mixture containing **carbohydrate**, protein and fat (12.56 kJ/ml) prior to aminophylline injection elicited increases of 29.6, 16 and 13.7%, respectively, for the 3 feeding regimens and a sustained supra-maximal **thermogenesis** in the fasted state. Since substrate feeding modulated aminophylline stimulated **thermogenesis** only in the fasted state when endogenous substrate reserves are diminished, it is indicative that both the magnitude and duration of aminophylline induced **thermogenesis** are substrate dependent.

L16 ANSWER 40 OF 49 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 1981:255101 BIOSIS
DOCUMENT NUMBER: PREV198172040085; BA72:40085
TITLE: THE GLYCO PROTEIN COMPOSITION OF PERIPHERAL NERVOUS SYSTEM MYELIN SUBFRACTIONS.
AUTHOR(S): LININGTON C [Reprint author]; WAEHNELDT T V
CORPORATE SOURCE: MAX-PLANCK-INST EXPERIMENTELLE MEDIZIN, FORSCHUNGSTELLE NEUROCHEMIE, HERMANN-REIN-STR 3, D-3400 GOETTINGEN
SOURCE: Journal of Neurochemistry, (1981) Vol. 36, No. 4, pp. 1528-1535.
CODEN: JONRA9. ISSN: 0022-3042.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
AB Two fractions were isolated by continuous density gradient centrifugation from total particulate matter of rabbit sciatic nerves: a minor fraction, B, consisting of small-sized membrane fragments and a major fraction, C, of characteristic multilayered myelin figures, with maxima at 0.38 and 0.58 M-sucrose, respectively. In comparison with C, fraction B was enriched in CNPase [2',3'-cyclic nucleotide 3'-**phosphodiesterase**] and alkaline phosphatase activities and the P0, 23K and Z proteins, but was virtually devoid of basic protein. The glycoprotein composition of all fractions was examined with 4 fluorescein isothiocyanate-labeled lectins (WGA [**wheat** germ agglutinin], Con A [concanavalin A], RCA-60 [Ricinus communis agglutinin] and U.E. [Ulex europeus agglutinin]). These revealed the presence of 6 glycoproteins in all fractions with similar lectin binding capacities and MW ranging 35,500-16,000, of which P0 was the predominant component. Material found on the heavy side of fraction C was characterized by the presence of a multitude of glycoproteins which bound variable proportions of the 4 different lectins, suggesting substantial variations in their **carbohydrate**

moieties. Their absence from the central portion of fraction C points to a location other than that of compact PNS [peripheral nervous system] myelin.

L16 ANSWER 41 OF 49 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 1982:157489 BIOSIS
DOCUMENT NUMBER: PREV198273017473; BA73:17473
TITLE: THE POTASSIUM THIO CYANATE EXTRACT OF PASTEURELLA-MULTOCIDA ELECTRON MICROSCOPY AND SUSCEPTIBILITY OF ITS IMMUNOGENIC ACTIVITY TO SOME PHYSICAL CHEMICAL AND ENZYMATIC TREATMENTS.
AUTHOR(S): MUKKUR T K S [Reprint author]; PYLIOTIS N A
CORPORATE SOURCE: COMMONWEALTH SCIENTIFIC AND INDUSTRIAL RESEARCH ORGANIZATION, MCMASTER LABORATORY, GLEBE, NEW SOUTH WALES 2037, AUSTRALIA
SOURCE: Journal of Comparative Pathology, (1981) Vol. 91, No. 3, pp. 427-438.
CODEN: JCVPAR. ISSN: 0021-9975.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
AB The immunogenic activity of a potassium thiocyanate extract of P. multicida type A was considered to be at least partially associated with a protein component as judged by the loss of protection and lack of development of bactericidal activity in mice immunized with the extract either digested with the proteolytic enzymes papain, trypsin, pronase and proteinase K or subjected to **heat** treatment at **temperatures** ranging from 56° C-121° C. Treatment of the extract with pepsin, **DNase** and RNase did not abolish its immunogenic activity. Treatment of the extract with sodium metaperiodate resulted in a partial loss of its immunogenicity, which suggests that probably **carbohydrates** either constituted additional immunogens or that the protective antigen(s) were glycoprotein in nature. Chemical analysis revealed the extract to contain proteins, lipopolysaccharide, DNA, RNA, and hyaluronic acid. Heterogeneity of the extract was further substantiated by polyacrylamide gel electrophoresis. Electron microscopy revealed that the extract contained fragments of membrane-like material, which were of cell wall origin. Passive immunization experiments revealed a linear dose-response relationship between the bactericidal titer of the specific antiserum and percent protection as judged by challenge infection with the homologous micro-organisms.

L16 ANSWER 42 OF 49 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 1980:266035 BIOSIS
DOCUMENT NUMBER: PREV198070058531; BA70:58531
TITLE: CHARACTERIZATION OF PNEUMOCOCCAL PURPURA PRODUCING PRINCIPLE.
AUTHOR(S): CHETTY C [Reprint author]; KREGER A
CORPORATE SOURCE: DEP MICROBIOL IMMUNOL, BOWMAN GRAY SCH MED, WAKE FOREST UNIV, WINSTON-SALEM, NC 27103, USA
SOURCE: Infection and Immunity, (1980) Vol. 29, No. 1, pp. 158-164.
CODEN: INFIBR. ISSN: 0019-9567.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
AB Purpura was grossly observable in albino mice 6-8 h after the i.p. injection of sterile, **DNase**-treated, cell-free extracts prepared by sodium deoxycholate-induced lysis, sonic disruption, Parr bomb

treatment, autolysis without sodium deoxycholate or alternate freezing and thawing of washed suspensions of Streptococcus pneumoniae type I. Cell-free extracts obtained from sonically disrupted, **heat** -killed cells (100° C for 20 min) did not contain purpurogenic activity. The reaction was maximal at approximately 24 h post-injection, started to fade slowly after 24-48 h and usually was not grossly observable by 4-6 days post-injection. The purpura-producing principle (PPP) in the cell-free extract was purified by sequential (NH4)2SO4 **precipitation**, protamine sulfate **precipitation**, Sepharose 6B gel filtration, **wheat** germ lectin-Sepharose 6MB affinity chromatography, RNase and trypsin treatment and a 2nd Sepharose 6B gel filtration step. The final preparation contained glucosamine (5.6%), muramic acid (8.0%), neutral **carbohydrate** (12.8%), phosphate (8.0%), orcinol-reactive material (6.0%) and Lowry-reactive material (1.6%) and was free of detectable amounts of DNA, capsular polysaccharide, neuraminidase, cytolysin and hyaluronidase. The isoelectric point and MW of the PPP were approximately pI 3.0 and several million daltons, respectively, and activity remaining in the supernatant fluid after centrifugation for 1 day at 105,000 + g. PPP activity was destroyed by incubation with egg white lysozyme and sodium metaperiodate but was resistant to trypsin, pronase, α-amylase, **DNase**, RNase, alkaline phosphatase, pancreatic lipase, 7% trichloroacetic acid, 6 M urea, autoclaving (121° C) for 30 min and mild acid and alkali exposure. The PPP may require intact β-1,4-glucosidic linkages for activity. Activity may be associated with pneumococcal peptidoglycan solubilized by the bacterium's autolysin.

L16 ANSWER 43 OF 49 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN

ACCESSION NUMBER: 1980:143097 BIOSIS
DOCUMENT NUMBER: PREV198069018093; BA69:18093
TITLE: ANTI TUMOR ACTIVITY AND LYMPHO RETICULAR STIMULATION PROPERTIES OF FRACTIONS ISOLATED FROM CORYNEBACTERIUM-PARVUM.
AUTHOR(S): CANTRELL J L [Reprint author]; WHEAT R W
CORPORATE SOURCE: ROCKY MT LAB, NATL INST ALLERGY INFECT DIS, HAMILTON, MONT 59840, USA
SOURCE: Cancer Research, (1979) Vol. 39, No. 9, pp. 3554-3563. CODEN: CNREA8. ISSN: 0008-5472.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH

AB Numerous studies have demonstrated that killed suspensions of C. parvum [Propionibacterium acnes] possess both lymphoreticular stimulatory and antitumor properties. In the present study, experiments were designed to isolate and characterize the component from C. parvum responsible for inducing stimulation of the lymphoreticular system and for inducing inhibition of progressive tumor growth. Fractions of C. parvum, prepared by hot phenol:water extraction of **heat**-killed bacteria, were tested in mice for lymphoreticular stimulation by measuring the degree of splenomegaly and spleen cell blastogenesis produced by an i.p. injection of the fractions. Antitumor activity was evaluated by measuring the extent of tumor growth after a s.c. injection of the C. parvum fractions admixed with either of 3 syngeneically transplanted murine tumors (B-16 melanoma, L1210 leukemia, or MC-93 sarcoma). Significant splenomegaly with concomitant increase in blastogenic activity was observed in mice treated with the residue after phenol:water extraction of C. parvum. The kinetics of development of splenomegaly and blastogenesis paralleled that observed by inoculation of whole organisms. In addition, significant antitumor activity, 80-100% inhibition of tumor growth, was observed in

mice inoculated with an admixture of tumor cells and the extraction residue. The antitumor activity of the residue was similar to that observed with whole cells. The extracts (aqueous and phenol phases) did not induce splenomegaly, increase blastogenesis, or inhibit tumor growth. Although purified cell walls had some antitumor activity (20-30% protection), the percentage of mice protected from tumor growth by cell walls was markedly less than that by whole organisms or the residue. Cell walls and/or protoplasm did not induce splenomegaly or increase blastogenesis. High antitumor- and splenomegaly-inducing activities of the residue were retained following chloroform:methanol extraction, sodium lauryl sulfate:pronase digestion, or sodium lauryl sulfate:pronase plus RNase;**DNase**:trypsin digestion, whereas these properties were significantly reduced after the residue was treated with metaperiodate, which resulted in a marked reduction in the **carbohydrate** concentration. Peritoneal cells from mice given an i.p. injection of whole organisms, phenol: water extraction residue, or periodate- or enzyme-treated residue were nonspecifically cytotoxic to B-16 tumor cells in vitro. Tumoricidal activity of peritoneal cells did not develop in mice treated with either the aqueous or the phenol phase from extracted C. parvum. Collectively, results from this study demonstrate that the component in C. parvum responsible for antitumor activity and lymphoreticular stimulation is, in part, **carbohydrate** in nature and that, although nonspecific macrophage activation by whole cells or the extraction residue may be important, it is not sufficient for inducing tumor rejection. The possibility that full activity may depend upon the integrity of cell walls is discussed.

L16 ANSWER 44 OF 49 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN

ACCESSION NUMBER: 1979:259248 BIOSIS
DOCUMENT NUMBER: PREV197968061752; BA68:61752
TITLE: INHIBITION OF TRITIATED THYMIDINE INCORPORATION IN CULTURED CELLS BY RAT KIDNEY EXTRACT.
AUTHOR(S): KLEIN K [Reprint author]; COETZEE M L; MADHAV R; OVE P
CORPORATE SOURCE: DEP ANAT CELL BIOL, SCH MED, UNIV PITTSB, PITTSBURGH, PA 15261, USA
SOURCE: Journal of the National Cancer Institute, (1979) Vol. 62, No. 6, pp. 1557-1564.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH

AB KCl extract from rat kidney, rat liver, and Morris hepatomas inhibited [3H]thymidine incorporation into cultured cells. Tissues came from male inbred BUF rats. The most pronounced inhibition was achieved with the kidney extract. Protein synthesis was not inhibited during a 24 h exposure of the cells to the inhibitor. Incorporation of [3H]deoxycytidine was inhibited, as was cell growth, when the kidney KCl extract was present for several days. [3H]thymidine incorporation was inhibited almost immediately after the addition of the extract. The inhibition was reversible. Regular [3H]thymidine incorporation was restored 24 h after removal of the inhibitor, which was neither arginase nor a thymidine-degrading enzyme. The inhibitor was **stable** to **heat** (80° C for 10 min) and resistant trypsin, pronase, **DNase**, and RNase. Exposure of the extract to proteolytic enzymes, hyaluronidase, and neuraminidase resulted in a loss of inhibitory activity only after extensive dialysis of the treated extract. The inhibitor appeared to be a mucoprotein in which the **carbohydrate** moeity may be responsible for the inhibition. The KCl extract also inhibited RNA synthesis and DNA synthesis by the de novo pathway. The inhibition of phosphorylation of thymidine appeared to be the primary action of the

inhibitor.

L16 ANSWER 45 OF 49 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 1980:128762 BIOSIS
DOCUMENT NUMBER: PREV198069003758; BA69:3758
TITLE: PURIFICATION AND CHEMICAL CHARACTERIZATION OF THE **HEAT** LABILE ENTERO TOXIN PRODUCED BY ENTERO TOXIGENIC ESCHERICHIA-COLI.
AUTHOR(S): KUNKEL S L [Reprint author]; ROBERTSON D C
CORPORATE SOURCE: DEP MICROBIOL, UNIV KANS, LAWRENCE, KANSAS 66045, USA
SOURCE: Infection and Immunity, (1979) Vol. 25, No. 2, pp. 586-596. CODEN: INFIBR. ISSN: 0019-9567.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
AB **Heat**-labile enterotoxin (LT) produced by a **human** strain of enterotoxigenic E. coli (286C2) was purified to homogeneity from pH extracts of fermentor-grown cells by ultrafiltration, (NH4)2SO4 fractionation, hydrophobic chromatography on norleucine-Sepharose 4B, hydroxylapatite chromatography and Bio-Gel P-150 filtration. Purified LT preparations exhibited biological activity comparable to that of cholera toxin in 4 bioassays specific for the 2 enterotoxins (Y-1 adrenal tumor cells, Chinese hamster ovary cells, pigeon erythrocyte lysates and skin permeability test). The overall yield of LT protein was 20%, which represented a 500-fold purification over pH extracts. A native MW of 73,000 was determined by gel electrophoresis. The toxin dissociated upon treatment with sodium dodecyl sulfate, pH 7.0, into 2 components with MW of 44,000 and 30,000. Purified LT preparations were remarkably **stable** over a wide range of storage conditions, **temperatures** and pH. The biological activity was increased by incubation with trypsin and completely destroyed by pronase and proteinase K, whereas **DNase** I, RNase and phospholipase D had no effect. The amino acid composition of purified LT was quite different from that of cholera toxin. Neither **carbohydrate** nor lipopolysaccharide was present in purified preparations. The purification scheme appeared applicable to LT produced by other **human** and porcine enterotoxigenic strains, but reflected the amount of LT produced by each strain. LT and cholera toxin share many common chemical and physical properties but must be purified by different techniques. [This may be relevant to the function of LT in diarrheal disease].

L16 ANSWER 46 OF 49 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 1979:245394 BIOSIS
DOCUMENT NUMBER: PREV197968047898; BA68:47898
TITLE: SOLUBLE SUPPRESSOR ACTIVITY OF CONCANAVALIN A ACTIVATED SPLEEN CELLS ON BONE MARROW DERIVED LYMPHOCYTE COLONY FORMATION IN-VITRO.
AUTHOR(S): CLAESSON M H [Reprint author]
CORPORATE SOURCE: DEP MED ANAT A, UNIV COPENH, 71 RADMANDSGADE, DK 2200 COPENHAGEN, DEN
SOURCE: Cellular Immunology, (1979) Vol. 42, No. 2, pp. 344-362. CODEN: CLIMB8. ISSN: 0008-8749.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
AB Supernates from concanavalin (Con) A-activated mouse spleen cell cultures suppress the formation of B [bone marrow-derived] lymphocyte colonies (BLC) in soft agar culture by 30-95%. Con A-induced BLC suppressive

culture supernates can be **heated** at 80° C for 1 h without losing activity. The BLC suppressive activity is eliminated totally by trypsin treatment and partly by treatment with β-galactosidase. Activity is unaffected by treatment with **DNAse**, RNAse and α-glucosidase. By ultrafiltration, the BLC suppressive factor(s) had MW greater than 300,000. BLC suppression may be mediated by a protein-**carbohydrate** complex. BLC suppression was obtained when normal spleen cells were preincubated in Con A-activated supernates for only 1 h at 37° C. BLC suppressor activity was absent in the supernatant fluid of Con A exposed anti-θ-treated spleen cells, nonadherent spleen cells, extensively washed spleen cells and spleen cells from nude (athymic) mice suggesting that cells responsible for Con A-induced BLC suppression are adherent, fragile cells of the T [thymus-derived lymphocyte] lineage. Con A-activated spleen cell supernates do not supress colony formation in soft agar by normal mouse granulocyte-macrophage precursors, by plasmacytoma cells, T lymphoma cells or by carcinoma cells. Colony formation by Abelson's murine leukemia virus transformed B lymphoma cells was suppressed by 95%, suggesting a relationship between this immature B lymphoma line and B lymphocyte colony-forming cells. Con A-activated spleen cell supernates do not suppress lymphocyte activation in liquid culture by phytohemagglutinin, Con A or [Escherichia coli] lipopolysaccharide. **Heat**-treated supernates which inhibited BLC development by 90-95% did not suppress the plaque formation by spleen cells immunized in vivo or in vitro by sheep red blood cells.

L16 ANSWER 47 OF 49 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN

ACCESSION NUMBER: 1980:155531 BIOSIS
DOCUMENT NUMBER: PREV198069030527; BA69:30527
TITLE: IMMUNOLOGICAL AND PHYSICOCHEMICAL PROPERTIES OF A HIGHLY PURIFIED ALLERGEN FROM DIROFILARIA-IMMITIS.
AUTHOR(S): FUJITA K [Reprint author]; IKEDA T; TSUKIDATE S
CORPORATE SOURCE: DEP MED ZOOL, KANAZAWA MED UNIV, UCHINADA, ISHIKAWA, JPN
SOURCE: International Archives of Allergy and Applied Immunology, (1979) Vol. 60, No. 2, pp. 121-131.
CODEN: IAAAAM. ISSN: 0020-5915.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH

AB Allergen in crude extract of D. immitis was purified and separated from Ig[immunoglobulin]G-inducing antigens by a combination of DEAE-Sephadex A-50 chromatography, Sephadex G-200 gel filtration and starch gel zone electrophoresis. The purified preparation was 1 protein band by sodium dodecyl sulfate polyacrylamide gel (SDS-gel) electrophoresis and 1 **precipitin** arc by immunodiffusion. MW of the purified allergen was approximately 20,000 by gel filtration and 15,000 by SDS-gel electrophoresis. **Carbohydrate** content of the preparation was apparently low, about 2%. The allergen was positively charged and its determinant group was protein in nature. It was resistant to tryptic, pepsic and chymotryptic digestion, periodate oxidation and **DNase** and RNase digestion but very sensitive to pronase digestion. Allergen was inclined to aggregate in buffered solution. It was very resistant to vibration, **heat** (80° C for 1 h), acid (pH 2.5) and alkali (pH 11.0) treatments. Rats and mice immunized with allergen developed only a reaginic antibody and no hemagglutination antibody.

L16 ANSWER 48 OF 49 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN

ACCESSION NUMBER: 1979:203530 BIOSIS

DOCUMENT NUMBER: PREV197968006034; BA68:6034
TITLE: EFFECT OF HYPO **THERMIA** ON THE METABOLISM IN THE LIVER DURING ITS PRESERVATION.
AUTHOR(S): KVITSINSKAYA E A [Reprint author]; KRIVULIS D B; SOROKIN YU A
CORPORATE SOURCE: DIV EXP SURG, CENT RES LAB, RIGA MED INST, RIGA, USSR
SOURCE: Byulleten' Eksperimental'noi Biologii i Meditsiny, (1978) Vol. 86, No. 8, pp. 179-182.
CODEN: BEBMAE. ISSN: 0365-9615.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: RUSSIAN

AB Experiments (20) were conducted on dogs. The effect of **hypothermia** of different **temperatures** (from 18-20° C and from 4-6° C) on the **carbohydrate** metabolism and the extent of solubilization of hepatic enzymes (lactate dehydrogenase, glutamate dehydrogenase, urokaninase, **DNase** and glucose-6-phosphatase) in perfusion-free preservation of the liver was studied. Preservation efficacy was assessed during the subsequent 2 h **normothermic** perfusion. A marked solubilization of the enzymes studied followed preservation of the liver at 18-20° C. This indicated the loss of intactness of the cell membranes during preservation. A moderate expenditure of the glucogen stores in the liver and of sugar in the perfusate followed preservation of the liver at a **temperature** of 4-6° C. An even suppression of hepatic metabolism and the prevalence of normal tissue respiration over glycolysis in the restoration of liver circulation is suggested.

L16 ANSWER 49 OF 49 MEDLINE on STN
ACCESSION NUMBER: 77056319 MEDLINE
DOCUMENT NUMBER: PubMed ID: 825781
TITLE: Tumor-associated antigen for cystadenocarcinomas of the ovary.
AUTHOR: Bhattacharya M; Barlow J J
SOURCE: National Cancer Institute monograph, (1975 Oct) 42 25-32.
Journal code: 0216026. ISSN: 0083-1921.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197701
ENTRY DATE: Entered STN: 19900313
Last Updated on STN: 19900313
Entered Medline: 19770125

AB An ovarian cystadenocarcinoma-associated antigen (OCAA) was found to be common to all serous and mucinous cystadenocarcinomas of the ovary. It was apparently absent in tissues of normal reproductive organs. **Furthermore**, OCAA was not detected in benign ovarian serous and mucinous cyst-adenomas or in any other gynecologic or nongynecologic cancers thus far tested. The antigenic determinant of OCAA was immunologically unrelated to the carcinoembryonic antigen, other known tumor antigens, or the histocompatibility antigens. We purified and partially characterized OCAA. The antigen was a high-molecular-weight glycoprotein soluble in 0.6 M perchloric acid. It consisted of about 50-60% protein (based on dry wt). Amino acid composition in OCAA was characterized by a high percentage of threonine, serine, proline, and valine. Galactose and N-acetylglucosamine were the principal **carbohydrate** constituents. The antigenic activity was resistant to treatment with trypsin and protease and also to treatment with **DNase**, RNase, and N-acetylneuraminidase. The antigenicity was

considerably reduced by mild periodate oxidation.